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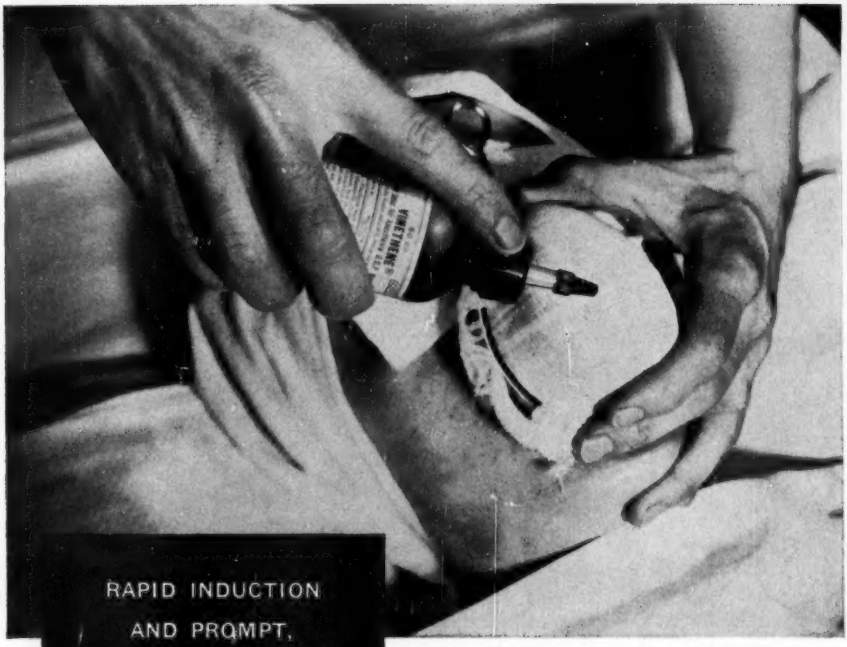

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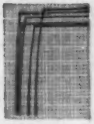

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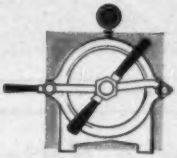

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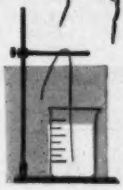

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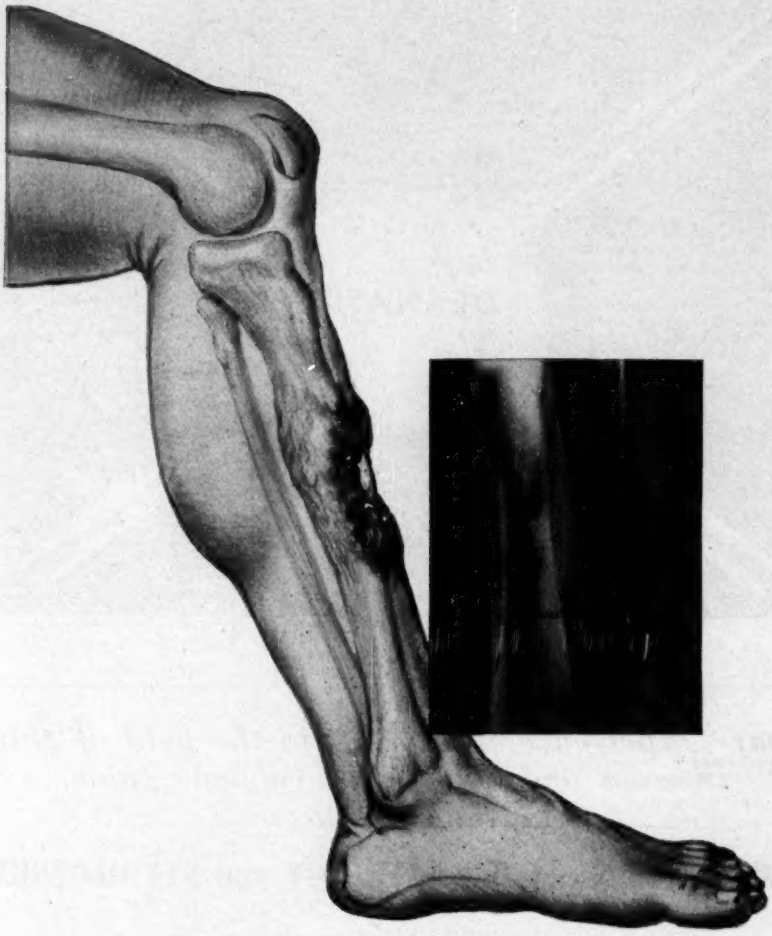

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Editorials

HOMEOSTATIC HEMOSTASIS

The Dynamics of Blood Coagulation

THE TECHNIQUES developed for the control of operative hemorrhage are sufficient that, save for accident, massive surgery is possible without excessive blood loss. These technical skills unfortunately are of little aid in patients who have an abnormal tendency to bleed due to a defective clotting mechanism.

While the biochemists and physiologists have greatly enriched our knowledge of blood coagulation, their findings have been applied primarily to in vitro observations. The basic scientists have proved the clotting mechanism to be more complex than had been appreciated in the past, demonstrating that several fields of scientific endeavor are involved. Among these are enzymology, physical and biochemical phenomena, thermodynamics, surface tension and the physiology and anatomy of the blood vessels.

We are told that in the absence of trauma or tissue breakdown blood within the circulation has no tendency to clot. The trigger mechanism that initiates coagulation is tissue injury either to the blood vessel or to its surrounding structures or the disintegration of platelets occasioned by their contact with foreign surfaces. In other words, coagulation is held in abeyance in its normal circulating environment or in a kinetic state, poised and ready to act when blood is shed or tissues are damaged.

The liberation of a substance by intracellular breakdown presumably activates a resting factor present in the plasma with the result that thromboplastin is formed. The framework of the present concept of coagulation can be best illustrated in the following three step reaction:

1. Prothrombokinase $\xrightarrow{\text{trauma}}$ Thrombokinase
2. Thrombokinase-prothrombin $\xrightarrow{Ca\ ++}$ Thrombin
3. Thrombin-fibrinogen $\xrightarrow{\text{Ac Glob}}$ Fibrin

Thromboplastin is unable to clot fibrinogen unless prothrombin is present. Prothrombin also is unable to clot fibrinogen unless it (prothrombin) is first converted to thrombin. The conversion of prothrombin to thrombin depends upon the presence of thromboplastin, and the thrombin thus formed then coagulates fibrinogen. In the last analysis, it is the fibrin clot which is responsible for biological hemostasis. The chain of events described above is only the basic framework by which blood coagulation occurs. It may be accelerated or retarded under certain circumstances.

Many of the reagents mentioned above have been isolated in highly purified states, and there is no doubt that the clotting reactions proceed essentially in the manner indicated in the diagram. However, there are certain questions that arise in clinical medicine pertaining to spontaneous and abnormal bleeding which theories both current and past fail to answer. For example, a patient with thrombocytopenia frequently develops manifestations of spontaneous bleeding. If, as we are taught, the platelets normally play only a passive role or are active only when trauma occurs, their disappearance from the circulation should not provoke petechial hemorrhage. Yet we all recognize that when the platelet counts rise in such patients, whether from splenectomy or not, the bleeding tendency disappears. A severe reduction of plasma prothrombin also is frequently associated with spontaneous hemorrhage. This type of bleeding ceases when the level of prothrombin activity is returned toward normal. Still we continue the belief that prothrombin is not converted to thrombin under normal circumstances in the circulating blood and that prothrombin is not normally activated or concerned with the prevention of spontaneous bleeding. The complete absence of fibrinogen is likewise said to give rise to spontaneous bleeding, and it is said that this may be controlled by the transfusion of fibrinogen in one form or another. Even so, we are taught that fibrinogen is not converted to fibrin in the circulation unless preceded by some form of trauma. Thus it has been presumed that the platelets, prothrombin, and fibrinogen in the normal circulation are inactive unless preceded by trauma. If these teachings are correct, spontaneous or nontraumatic hemorrhage cannot possibly occur even though platelets, prothrombin, and fibrinogen are entirely absent from the circulation. Since this is an erroneous conclusion, how can we then explain the differences between the theoretical concept and practical experience?

From these queries, it is clear that we are overlooking some fundamental mechanism and that this oversight is a stumbling block to our better understanding of prevention of spontaneous bleeding and of the true nature of the fluid state of the circulating blood. It is thus self-evident that we must re-examine our facts, hoping to find therein new laws and general principles that will harmonize these laboratory data with clinical experience.

Nearly all investigators hold to the belief that blood remains fluid only because it is not disposed to clot under normal circumstances or that clotting in the circulation is prevented by the action of some postulated but as yet unfound anticoagulant. In other words, it is assumed that the clotting mechanism is kinetic in its natural state and that it is only dynamic insofar as clotting occurs after trauma, damage to blood vessels, stasis, etc. This concept appears to me basically to be unsound and unique in the annals of physiology. After inquiring of my colleagues in biochemistry and physiology, I have been unable to locate evidence in support of any other similar biochemical or physiological reaction which is kinetic and only kinetic in its natural state. If this is true, why is it not prudent to investigate the possibilities of a dynamic blood coagulation, a coagulation which is carefully regulated by inhibitors and accelerators? The term "dynamic" as employed here would imply a continual slow coagulation, constantly occurring through the entire vascular system and that this dynamic process is essential to the prevention of spontaneous hemorrhage. This point of view would reconcile the differences between the facts

established by in vitro studies and those established by clinical observation. In brief, the cause of spontaneous bleeding and its relationship to the clotting mechanism would be evident.

There are many reasons to suspect that a dynamic coagulation may exist and that trauma merely accelerates this process. For example, platelets, prothrombin, and fibrinogen are turned over within the body within a period of two to three days. Whether this continuous turnover represents the utilization of these substances in a dynamic coagulation is not known. It is not known whether this postulated dynamic process would prevent bleeding by depositing a thin layer of fibrin along the vessel wall or whether microscopic bleeding normally occurs, and, in the presence of an abnormal clotting mechanism, precedes clinically evident hemorrhage.

There has been described an enzyme (fibrinolysin) in plasma which digests fibrin. Thus there would seem available the mechanism which could normally remove any fibrin formed within the vascular bed. Spontaneous hemorrhage has occurred when the rate of this enzymatic reaction has proceeded too rapidly.

It may be of some interest that the blood of the dog can be completely defibrinated by the slow intravenous injection of either thromboplastin or thrombin with survival of the animal, providing adequate pressure is maintained at the point of needle puncture until new fibrinogen is formed and deposited at the site of vessel puncture. We have been able to perform this experiment in our laboratory, administering these agents to dogs over a period of 30 to 60 minutes. This would seem to represent the maximum rate at which intravascular coagulation can be accelerated without fatality from intravascular coagulation. In the case of deficiency of platelets, prothrombin, or fibrinogen, the rate of coagulation theoretically would be retarded and therefore give rise to spontaneous bleeding.

The concept of a dynamic coagulation implies that the clotting mechanism is essential for the prevention of spontaneous bleeding and that the blood is not permanently fluid in the sense that it has been considered in the kinetic theory. While there are many data to support the dynamic concept, there are many questions yet to be answered before this postulated mechanism can be accepted as fact. Nevertheless, the failures of the kinetic theory are sufficient that it can no longer go unchallenged even though its origin dates back to the time of Aristotle.

J. Garrott Allen, M.D.

THE SURGICAL RESIDENT

Presidential Address

WALTER G. MADDOCK, M.D.
CHICAGO

IN PRESENTING this address, I am deeply conscious of the high honor conferred in electing me your President. My predecessors have been master surgeons and great teachers, and I only hope that I can approach their standards. Let me assure you that it has been gratifying to serve the Central Surgical Association, an active, vigorous, and dynamic group with the purpose of bringing together fellow surgeons for the presentation and exchange of surgical ideas. An ever-growing association tradition enhancing the pleasure of these meetings has been enjoying the fellowship of one's colleagues.

The subject of my address is "The Surgical Resident." A great deal has been written about the training of this young man for his ultimate place in the surgical affairs of the community, and all thoughtful medical educators agree that the apprentice system is ideal for his development, providing always that the teacher is ethically as well as surgically qualified. Wangensteen has stated concisely that the development of the neophyte is not a process that can be hurried, but one which must come naturally through a certain sequence of events, which by no means is the same for all individuals. "This development has to do with the young surgeon becoming steeped in the practices, techniques and procedures as well as the general approach of a surgical service to problems." [1]

My particular thoughts in writing this address are on some of the qualifications, duties, and performance of a top-grade surgical resident. There is a paucity of medical literature on this subject, most essayists discussing the facilities and plans for the resident's apprenticeship but having less to say about the individual himself. Since the good resident while learning surgery is also a beginning executive, I have looked at the writings of lawyers and business executives to discover what qualities they also consider essential for success.

GENERAL QUALIFICATIONS

Intelligence.—This should not be a difficult requirement for the surgical resident, considering the selective process he has been subject to from h[illegible] school on. Most medical students are in the higher intelligence brackets and n[illegible]e close to a B+ scholastic rating before entering medical school. That the surgical resident does

Read before the Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

1. Wangensteen, O.: The Surgeon and His Trust, Surg., Gynec. & Obst. **84**:567-578 (April 15) 1947.

not need to be in the top 10% of his medical class is indicated by my knowing many excellent residents who were not top scholars yet had many other desirable traits for success. It has been pointed out that intelligence and scholarship are by no means synonymous. The first is an indication of certain innate traits or capabilities, whereas the latter is a measure of actual accomplishments in school. Although in general it is agreed that scholarship and mental alertness show a high correlation, we all know of exceptions in which a student somewhat below the highest level of intelligence makes excellent grades by dint of dogged persistence and hard work, while a truly brilliant man, because of indifference or lack of interest in certain studies, turns out to be only a mediocre student. University teachers are prone to exaggerate the importance of intelligence. It is indeed likely to be the chief factor in their own success, and they tend to estimate the effectiveness of their colleagues in terms of intellect alone. They rank students in order of their ability to master and manipulate ideas. In the world of business, on the other hand, success is first of all a matter of getting things done. This does not mean that business firms fail to give consideration to the academic records of the college men they employ. On the contrary, they are coming more and more to regard the grades received in college not only as the best available objective measure of intelligence but as a good indication of actual performance on the last "job."

In general, it is apparent that the opinions of executives come close to confirming the judgment of educators as to what the ends of higher education should be. Educators recognize that the "learning" of subjects in the curriculum, the memorization of knowledge or information, is in reality of subordinate importance to the development of disciplined habits of thought and work and the capacity for accurate and original reasoning. These, along with sound judgment, are the very pillars of a successful career and need be present in high degree in the young resident.

Organizational Ability.—A surgical service is a theater of action and requires organizational ability. Things are being done, and usually in considerable volume. To run the service well and to avoid errors, there must be organization, which means planning. First things must be done first. The very essence of the successful care of a number of patients is the high percentage of thought and time given to those with diagnostic problems and to the few who are seriously ill. The remaining majority present simpler problems and progress nicely. In order to do the most for each patient, the resident and his intern should feel full responsibility for his care: Histories and physical examinations should be checked, the results of laboratory studies reviewed, and all those connected with the case should commit themselves to a diagnosis on the chart. This should be checked with the attending surgeon and treatment planned; it is often highly instructive and adds greatly to the interest of ward rounds to compare these original opinions with the final diagnosis.

The resident must know the progress of his patients, not in vague generalities but in sufficient up-to-the-minute detail to give a concise report to his surgeon at any time. If he is wise, he will take nothing for granted but will check on practically everything. He will avoid most complications by anticipating them and taking appropriate countermeasures. In regard to this alert, anticipatory attention, a friend of mine who is a distinguished lawyer gave me his account of the "second-chair man," who, you will find, is somewhat analogous to a good resident. This individual is the first assistant to the trial lawyer at the trial and

occupies the second chair at the law table. He may or may not have worked up the case, but he knows all about it, and at the trial it is his job to keep the case in order. He is expected to have reviewed the courtroom in advance in order to know its acoustics. He should have arranged all technical information, say from engineers or physicians, so that a jury can understand it. Possible objections to evidence or documents must be anticipated and memoranda of authorities be on hand to support contentions. He must bring into the courtroom pins, paper clips, poster tags, tags with strings on them, etc., for the careful marking and arranging of all exhibits, so that there will be no interruptions or pawing for data at the last minute. And the legends attached to these exhibits must be descriptive enough to indicate just what they are. The second-chair man keeps readily available notes when his advocate is cross-examining a witness. He should be ready with occasional instantaneous help by whispering an important point. And almost of most importance, he must see that something of consequence is not overlooked. Fine suggestions often come from the second-chair man, and many lawsuits have been won by ideas arising from his alertness and possible different point of view. He has one of the toughest jobs in the field of advocacy, but there is no place where one can learn more of good judgment, and the "how" of doing things, than in the second chair.[2]

This attention to details at all times is highly important in surgery, since the smooth progress of the service and possibly the life of a patient is at stake. Surgical treatment is more concentrated than medical treatment: More things happen in a shorter time, and it is impossible to do an operation over again without expensive and harmful effects on the patient.

IN THE OPERATING ROOM

The marks of a good resident are apparent in the operating room, where his fundamental job as first assistant is to make it easy for the surgeon to carry out the operation. Every procedure here will be facilitated by his punctuality, his knowledge of what is about to be done and the proper ways of carrying it out, his alertness to aid in the various steps, and the skillful use of his hands.

Punctuality.—Like other things, operations should start on time, and they do not do so of their own accord. There is no place for the laissez-faire attitude, and the dilettante is not to be tolerated. Drive and organized energy are needed to get things done, and preparatory steps should progress so that when the surgeon puts on his gown and gloves the field is set and ready to go. For a job involving many persons this is easier said than done, but a good resident will accomplish it regularly by having the patient in the operating room on time, the assistants there, the extra equipment, such as Wangensteen tubes and suction apparatus, and x-ray films on hand and in place, the anesthetic started, administration of intravenous fluids begun, and the patient in position and draped the way the surgeon likes it done. This requires teamwork, and it can be arranged for the benefit of everyone concerned.

Reviewing the Operation.—Books have always been the friend of the doctor, and here again a close companionship will be helpful. Reading about unfamiliar procedures the night before enhances the teaching value of an operation and should materially aid the resident's ability to assist. This means that he should have the

2. Haight, G. I.: The Second Chair Man, read before the Chicago Bar Association, Jan. 25, 1941.

right volumes in his room, readily at hand, to tell the steps to be used and the dangers to be avoided. Even a brief look at his favorite anatomy will review the structures of the area, make the operation more intelligible, and offer a chance to exhibit knowledge beyond the ordinary, should the surgeon quiz a little. Simple and logical as are these suggestions, they are too seldom employed, even in these days of keen competition for advancement up the ladder of surgical progress.

Alertness.—A good surgical operation is a symphony of teamwork, with the assisting resident the first violinist. He so often means the difference between a smooth performance and a poor one, between mutual satisfaction and disharmony. As the surgeon proceeds, the assistants should aid in keeping his movements running easily to the completion of the whole performance. Too slow a tempo retards the surgeon's progress. The assistant may watch the surgeon's actions without being alert to his immediate part in the procedure, and thus require frequent reminders about obvious things to do. An illustrative and common error is to watch the surgeon tie a knot and yet not have scissors in hand to cut the suture.

Manual Dexterity.—It is generally the rule that the more a resident assists skillfully, the more he is allowed to do. Some use their hands well naturally, some learn this art, and some are confirmed clumsy fellows who will simply not make the grade. There are so many movements to make with grace and precision: a bleeder to grasp with just the tip of the forceps; a needle to be pulled through in the line of its curve instead of being worried out; the field to be kept free from unnecessary staining with blood, and hemostats to be removed with firm sureness. A good resident must be able to tie sutures securely and in several ways. A particularly thoughtful fellow will use the method employed by the surgeon with whom he is working and be quite able and ready to change when he changes surgeons. Above all, this important procedure in surgical technique must be learned not in the operating room but through continued practice at odd moments in the resident's room and elsewhere. Hands are beautiful tools, and both should be used. When not employed, they should rest quietly but be alert for the next assist.

WORK ON SURGICAL PROBLEMS

Study of surgical problems may seem a large order to the busy resident, and truthfully there are times when little can be done because of the press of other duties. But some period during the resident's training should be set aside for the engagement of the mind with a surgical or allied problem. This is best done by a year in the laboratory, although there are other ways of carrying it out. The results obtained may or may not be of importance in themselves, but to be concerned with an idea which may possibly add to the sum total of surgical knowledge, to have searched the literature, cudgeled up some originality in thought, carefully observed and collected data, analyzed the tabulation, and arrived at sound conclusions is an experience of inestimable value. And of no less importance to the neophyte is the preparation of the report. Be it published or not, it is quite unlikely to prove acceptable to the chief if lacking in good form and expression.

Facility in oral and written expression is something to be expected of college graduates, but sometimes it is woefully lacking. Many English courses have been taken, but too often as a separate study without effect on the general bearing of

other courses. It has been aptly stated that "to expect two or three courses in composition and public speaking to correct faults in expression which are allowed to flourish unchecked in other courses and in the daily lives of students is tantamount to expecting ten minutes of setting up exercises each morning to keep a man healthy throughout a lifetime of dissipation." It will not do, for nothing short of insistent and continuous high standards of oral and written work will suffice. How commonly this expression is used erroneously: "The patient *was operated* that afternoon." One operates a street car or an automobile, whereas, "The patient *was operated upon* that afternoon" is correct. So, for the resident, proper command of the English language is essential, and respect for this accomplishment is heightened by the five to seven times the research paper usually has to be written before final acceptance.

AS A TEACHER

The resident has a job to do for himself in learning to become a surgeon and no less of a job to do for others, since he is a supervisor and teacher in many of his capacities. This holds true for the assistant resident, but even more so for the chief resident. The latter should have acquired a good surgical technique and be capable of readily doing the common operations. Even the more intricate procedures, after careful study, can be performed safely and very creditably.

Now, as head of the surgical house staff, the chief resident should be responsible for and take an active part in carrying out the teaching schedule. This is an opportunity thoroughly grasped by the exceptional man, since his institution is vitally interested in teaching, and the process will broaden his own development. To be a good teacher he must know his subject thoroughly, and, of equal importance, he must continue to learn it. The second requirement, that of liking the subject, should come easily and result in vigor, enthusiasm, and imagination in his teaching methods. The third essential is to like the pupils, and where can one find a more energetic and receptive group than medical students in their clinical years and young doctors? The emphasis of teaching at this level should be not on the stuffing in of factual material followed by classroom repetition, but on the analysis of collected material and the development of rational judgment.

Whether the resident continues in an academic career or enters private practice, the teaching experience will be ever valuable, for he should have learned to guide and counsel people, to think on his feet, and to speak clearly and forcefully.

AS A DOCTOR

No matter what his development as a surgeon, the resident must never forget that he is a doctor and, as such, will be continually looked to for hope, understanding and sympathy. No patient should become a number and no doctor a machine. The personal element is powerful, and among life's critical inspections none is more searching than the patient's first look at his surgeon. The patient commonly rates the risk of operation high and is frequently fearful for his life. He usually will have heard of the surgeon's skill, but he hopes to see for himself the reassuring signs of a confident manner and cheerful mien, to hear an intelligent discussion of the treatment planned, and to feel the surgeon's personal interest in his illness.

CONCLUSION

I have written this address with warm affection for the surgical resident, not only because of the enduring memories of my own residency under Dr. Fred Coller at the University of Michigan but also because of the residents I later helped to train. These young men are professional sons, whose needs and companionship lift surgery from a routine of patients to a broad stimulating activity. Wangensteen has well said, "The teacher who leaves no pupils or intellectual progeny, has not been fully alive to his responsibilities or wholly faithful to his trust."[1] Gallie thoughtfully states that "The ideal of the teaching surgeon should be not how skillful and impressive he can make himself by constant practice and repetition, but how many young men he can train to be as good or better than himself."[3]

Most of the members of this young Association were surgical residents not so long ago, and practically all are now engaged in training residents. It is often hard work, but the job is ours, and there is no more satisfying reward than to play a part in spreading the principles of sound surgery over an ever-increasing sphere of influence.

250 E. Superior St.

3. Gallie, W. E.: Ideals in Surgery, Surg., Gynec. & Obst. **84**:513-518 (April 15) 1947.

PLASTIC SPONGE WHICH ACTS AS A FRAMEWORK FOR LIVING TISSUE

Experimental Studies and Preliminary Report of Use to Reinforce Abdominal Aneurysms

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SURGEONS have learned that certain nonabsorbable foreign materials are occasionally useful in surgical reconstruction of certain organs and structures of the body. They have learned that although the foreign material is inferior to living tissue in many respects and never becomes truly a part of the body, materials such as tantalum, vitallium, stainless steel, polyethylene, polyvinyl and methyl methacrylate will often serve in place of living tissue to fill defects or correct deformities. The limitations of foreign materials used at present are well recognized. Foremost of these limitations, and common to all materials in widespread use, is failure to become united with surrounding living tissue. In certain circumstances this characteristic is not a limitation but a desirable quality, in others it is more or less of a handicap, and in still others it constitutes an objection to the use of foreign material. Hence, the finding of nonabsorbable materials, which not only are stable and biologically inert but also become part of the structure of living tissue and could thus be used for procedures in which firm union with adjacent tissue is necessary, would be of interest to surgeons.

In the course of our experimental studies on the suitability of synthetic plastics for various purposes in surgery we attempted to obtain inert plastics in the form of a sponge. Several materials were tested and found unsatisfactory. Eventually, we learned of, and were able to obtain, a plastic sponge which promised to be suitable.[1] Polyvinyl sponge, like polyvinyl copolymer tubing and film which we and others had found to cause little tissue reaction, is made from polyvinyl alcohol. It is made by a special process in which polyvinyl alcohol is foamed and then hardened with formaldehyde. Sponges of uniform texture and high quality are available commer-

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From the Division of Experimental Medicine, Mayo Foundation (Dr. Grindlay), and the Division of Surgery, Mayo Clinic (Dr. Waugh).

The plastic sponges used in this study were kindly supplied by the manufacturer, Ivano, Inc., 123 East Twenty-First Street, Chicago 16, and are available for the medical profession from Clay-Adams, Inc., of New York City.

1. Grindlay, J. H., and Clagett, O. T.: A Plastic Sponge Prosthesis for Use After Pneumonectomy: Preliminary Report of an Experimental Study, Proc. Staff Meet., Mayo Clin. **24**:538-539 (Oct. 12) 1949.

cially because they are sold widely for cleaning purposes. They can be wet and wrung out like sea sponge or chamois skin. Sponges which are made for such uses are colored during manufacture by the addition of pigments.

CHARACTERISTICS OF POLYVINYL SPONGE

Physical Characteristics.—The color of pure polyvinyl sponge is white. Its surface has the appearance of the cut surface of a slice of white bread. The texture, which can be varied considerably in the course of manufacture from fine to coarse but which was fine in the case of sponges that we used, is like that of some loaves of bread, fine and uniform except for an occasional larger hole. When it is dry, polyvinyl sponge is hard and rigid. Dry sponge has great mechanical strength and is not brittle. Moist sponge is resilient and soft. It is easily compressed and, when pressure is released, instantly springs back to its former shape. Like rubber sponge, moist polyvinyl sponge is elastic and tough and has great tensile strength. Dry sponge can be cut with a heavy knife or, better, with a saw. Moist sponge can be cut easily with a sharp knife or scissors.

Polyvinyl sponge is very light, its density being about 0.05. Its other most prominent characteristic is its great affinity for water. Not only does the substance of the sponge become permeated with water and swollen, but the sponge will hold as large a volume of water as will a sea sponge. If it is wrung out and is wiped across a wet surface, it will leave the surface dry. The sponge itself dries slowly, as though reluctant to give up moisture. During drying some shrinkage occurs.

Temperatures up to 120 C. have no effect on polyvinyl sponge, but higher temperatures cannot be withstood for long periods of time. After one hour at 160 C. the sponge begins to turn brown. When a sponge is boiled in water for the first time there is slight shrinkage, but subsequent boilings do not cause further shrinkage. If the sponge is compressed by some object while it is in water heated above 95 C. and if the compression is maintained while the sponge is cooled to a temperature less than 95 C., the deformity caused by the compression will remain. The deformity can be removed and the sponge restored to its original shape by heating it again in water above 95 C.

Chemical Characteristics.—Polyvinyl sponge has no odor or taste. It can be ignited with a match and will burn quietly with a yellow flame which can easily be completely extinguished. At ordinary temperatures polyvinyl sponge is inert to almost all chemicals. It is not affected by strong or weak alkali, weak or moderately strong acids, organic solvents, formaldehyde or glycerols. It is adversely affected by concentrated acid, by aqueous solutions of certain organic solvents such as alcohol when the concentration of the solvent is between 30 and 70%, and by strong solutions of certain synthetic detergents.

PREPARATION OF SPONGE FOR SURGICAL USES

Only pure, white, polyvinyl sponges which contained no color pigment or other impurities were used in this study. We used the standard, commercial size of sponge, a size and shape approximately that of a brick (17.5 by 9.5 by 6.5 cm.). Until the sponges were used, they were kept in the sealed, airtight, plastic bags in which they were furnished by the manufacturer. Care was used to protect sponges

from dust and to avoid soiling them in any manner while they were being prepared for sterilization. After a sponge had been removed from its package, it had to be washed thoroughly in order to remove a hygroscopic substance added by the manufacturer to keep the sponge moist and soft. This was done by soaking and wringing out the sponge several times in as many changes of tap water and then leaving it overnight in running water.

Before sterilization large sponges were cut to the approximate size in which they were to be used. A special technic was devised for cutting sponge into sheets of various but uniform thicknesses (Fig. 1). The first step of the technic was to soak a sponge in a warm and strong solution of gelatin. The sponge was then squeezed gently to remove excess gelatin solution. Then the sponge was placed in the freezing compartment of a refrigerator and allowed to remain there overnight. The frozen

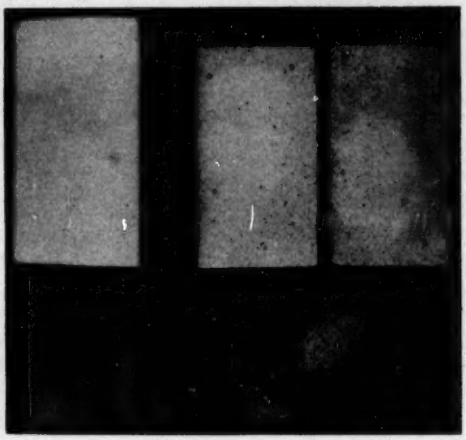

Fig. 1.—A polyvinyl sponge (upper left) and four slices of sponge varying in thickness from 1 to 3 mm.

sponge could then be cut into uniform slices having the required thickness and as thin as 1 mm. by slicing it in an ordinary electric meat slicer. Washing in lukewarm water removed gelatin from the slices.

Sterilization.—Sterilization of polyvinyl sponges was accomplished by boiling them for 30 min. Clean tap water and clean vessels were used. Vessels had well-fitting lids and were large enough so that the sponge could float freely without touching the vessel and thus not be deformed by being pressed against the wall while being boiled. Ordinarily, the sponges were boiled late in the day before they were used so that they could cool overnight in the water in which they were boiled. If a sponge was boiled just before an operation, it was not handled until it and the water in which it was boiled had been cooled by the addition of cold sterile water, or by cooling the entire vessel in cold, running water.

The boiled and cooled sponge was then wrung out, soaked in sterile isotonic sodium chloride solution and wrung out again. It was now ready to be placed in the animal.

Shaping and Molding of Sponges.—For most purposes the piece of sponge which is to be implanted can be cut to the desired size and shape with scissors. Its flexibility and natural tendency to take the form of the tissue on which it rests make this method of shaping sufficient for most purposes. However, accurate molding of polyvinyl sponge is possible and simple. Our method is based on the observation that any deformation which is made while the sponge is in boiling water and is maintained while the sponge is cooled becomes permanent. Thus, if a sponge is lifted from boiling water in a mold against the sides of which it presses, it will have the shape of the mold after it cools (Fig. 2). Because excessive compression of

Fig. 2.—Molded polyvinyl sponge. These pieces of sponge were first roughly shaped by cutting with scissors and then finished by the heat-molding process described in the text. At the upper left is a rib-shaped sponge. The other sponges are the shape which were implanted in the breast or forehead region.

polyvinyl sponge impedes ingrowth of tissue, we learned to shape the wet, cool sponge before it was boiled to a rough approximation of what was desired. Perfection of contour could then be achieved by heat molding with a minimal degree of compression of sponge.

RESULTS

Polyvinyl sponge was implanted surgically in 37 areas in a series of 28 dogs. All operations were performed with the animal under ether anesthesia and with aseptic surgical technic. At various lengths of time after the sponge had been implanted, either the sponge and the surrounding tissues were excised en bloc at a second operation or the animal was killed. Gross examination of the sponge and the adjacent tissues was accomplished by careful dissection. Typical portions of sponge and marginal tissue were examined after histologic preparation.

Sponges which had been shaped to fit the empty pleural cavity after pneumonectomy [2] were sutured in the empty pleural cavity of 11 dogs. In two dogs a portion of one rib was excised and a molded rib of sponge was placed in the rib bed. Most of the right hemidiaphragm was excised in two dogs and replaced with a sheet of sponge having about the same thickness as the diaphragm. The anterior sheath of the rectus muscle was removed and replaced by a sheet of sponge of the same thickness in six dogs. Sponges of various size and shape were placed in subcutaneous tissue in six dogs; in the same dogs a cone-shaped molded sponge was also placed under a breast nipple. Two dogs had conical sponges sutured to periosteum between the orbital ridges of the frontal bone. Thin plates of sponge were sutured to the surface of the ear cartilage in two dogs.

No systemic reaction to the presence of the sponge was noted at any time in any of the experiments with the exception of two in which sponges were placed subcutaneously immediately beneath the skin incision. Local tenderness or induration of overlying tissue was never observed. In experiments in which the sponge was visible or could be palpated it seemed to remain the same size. Fluid could never be felt about the sponge, and roentgenograms of the chest did not show free fluid when sponges were placed in the diaphragm or the rib bed. Gradually the sponges became firm. The degree of firmness which the sponge mass eventually had was approximately that of a mass of fibrous tissue of the same shape and size.

With the exception of certain experiments the implanted sponges did not become fixed to surrounding tissue, even though the sponge itself contained blood vessels and connective tissue. For example, sponges placed in subcutaneous regions were always freely movable with respect to both the overlying skin and the underlying fascia. When sheets of sponge were sutured to muscle, fascia, cartilage, periosteum or pleura, they became firmly fixed to these tissues but could be moved freely in respect to other tissues with which they were in contact. The skin covering subcutaneously placed cone-shaped sponges on the forehead or the abdominal wall remained freely movable and showed no tendency toward inflammation or ulceration, even when it covered the rather pointed apex of the cone. Attention should be called also to the fact that none of the animals paid any attention to the implanted sponges, including the conical sponges placed between the eyes or in the abdominal wall.

Gross pathologic examination was made after removal of the sponge at a surgical operation, or at the time of necropsy after the animal was killed, in the majority of experiments. Sponges are still in situ in one experiment each in which the sponge was placed on rectus abdominis muscle, diaphragm, ear and forehead; two experiments in which conical sponges were placed under a breast nipple and seven experiments in which a sponge was placed in the pleural cavity are being continued. All 13 of the experiments in which sponges are still in situ are now of between one and two years' duration. We should like to continue a few experiments several more years. The shortest time for which a sponge was left in place before it was removed was one month. Examination at one month was made in one experiment in which the sponge was sutured to rectus muscle and in two experiments each in which it was placed subcutaneously or under the breast. One of the animals with

2. Grindlay, J. H., and Clagett, O. T.: Unpublished data.

a sponge in the pleural cavity was killed two months after operation. The remaining 18 experiments were terminated and pathologic examination was made between six and 18 mo. after operation.

Thorough gross examination was made after the mass of tissue containing the sponge had been fixed in formaldehyde for a few days. After fixation, tissues maintained their relationship to the sponge. Dissection showed that the sponges were in each case surrounded by a thin and delicate fibrous semitransparent capsule which was firmly adherent to them and could not be pulled away. The surface of the sponge was plainly visible through its capsule. Wherever the sponge had been sutured to tissue, rectus muscle, periosteum, ear cartilage or pleura, the fibrous capsule could not be separated from the tissue. In other places the fibrous capsule was separated from adjacent tissue by a loose and relatively avascular areolar tissue. The implanted sponge had the consistency of fibrous tissue and a light pink color. Its texture appeared the same as when it had been implanted. Cutting of the sponge

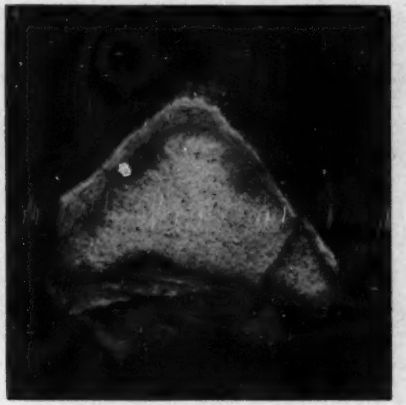

Fig. 3.—A section through a sponge which was placed under a breast nipple. The sponge was loosely attached to overlying skin and underlying fascia.

with knife or scissors was more difficult, when compared with a moist, fresh sponge, because of greatly increased resistance. The cut surface of the sponge mass showed that the pink color extended uniformly through the sponge; the texture of the cut surface was little changed, the empty spaces being present but smaller than when the sponge was inserted. When pressure was applied to the cut surface, thin pink fluid appeared at the point of pressure. When pressure was released, the fluid disappeared instantly. Sponges which have been removed and examined have shown no evidences of deterioration or change in physical properties.

Certain gross findings pertain only to the site of implantation and the method of fixation of the sponge. Where the rectus fascia had been replaced by a thin sheet of sponge, the sponge was firmly united to surrounding deep fascia, making the deep fascia a continuous layer. It was less adherent to rectus muscle than to fascia and only loosely adherent to superficial layers. Pieces of sponge which had been placed but not sutured in position in subcutaneous regions became loosely bound to

skin and fascia (Fig. 3). The conical sponge which was sutured to the periosteum of the frontal bone and the thin sponge sutured to ear cartilage became firmly fixed to these tissues, but overlying skin could be moved back and forth. There were no pleural adhesions and the underlying pleura was not thickened in the experiments in which sponge was sutured in the periosteal bed after rib resection (Fig. 4). There was a firm union between periosteum and sponge but no gross evidence of bone formation. The sheet of sponge used to replace most of the muscular portion of the right diaphragm formed a continuous layer with the diaphragm. No hernia was present, and the sponge did not appear stretched. From the midline the sponge was covered on both sides as far laterally as the outer third of diaphragm by pleura and peritoneum. The remainder of the abdominal surface was adherent to the fundus of the stomach while the thoracic surface was adherent to the lateral chest wall. The large, lung-shaped sponges which had been placed in the pleural cavity after pneumonectomy were fixed firmly to the chest wall. On the diaphragmatic aspect

Fig. 4.—Pleural surface of the chest wall in a dog in which a sponge was placed in the periosteal bed after rib resection. A section from the center of the sponge was excised for histologic study. The pleura covering the sponge appears normal.

the fibrous capsule of the sponge was covered with a smooth and glistening layer of pleura. The mediastinal surface was loosely adherent to structures of the mediastinum.

In the two experiments in which sponges were placed subcutaneously immediately beneath a skin incision, a corner of the sponge was noticed protruding from the otherwise healed skin incision two months after operation. The surrounding edge of skin was slightly raised and indurated, but exudate or granulation tissue was not observed. These dogs were watched for four more months, during which time the sponges gradually became a little more exposed. When the sponges were removed, it was discovered that a few millimeters beyond the edge of the exposed portion of sponge all evidence of a mild, chronic inflammatory reaction ceased.

Histologic examination revealed few things which were not common to all experiments. A typical section (Fig. 5) of sponge and adjacent tissue showed no evidence of previous inflammatory reaction. Outside of the sponge capsule was normal muscle, pleura, cartilage, periosteum, fat or areolar tissue. The capsule con-

sisted of oriented bundles of collagen fibers in which were a few scattered nuclei. The innermost layers of the capsule merged with bundles of collagen fibers in the spaces of the sponge. The sponge, which did not tear or fragment when it was cut with the microtome, had the appearance of a strange but somehow normal-appearing organ. Irregular but for the most part straight-sided spaces which communicated with each other by junctions at irregular angles occupied from a half to two-thirds of any microscopic field. In sections stained with hematoxylin and eosin the spaces were colored faint blue and were homogeneous. Under higher magnification the faintly blue areas were faintly discernible as masses of closely packed bubbles. The strange histologic picture of the substance of the sponge was no more remarkable than the appearance of more recognizable cellular tissue which fitted into the spaces not occupied by sponge substance. Sections stained with hematoxylin and eosin showed, in such spaces, bundles of collagen fibers around large spaces the walls of

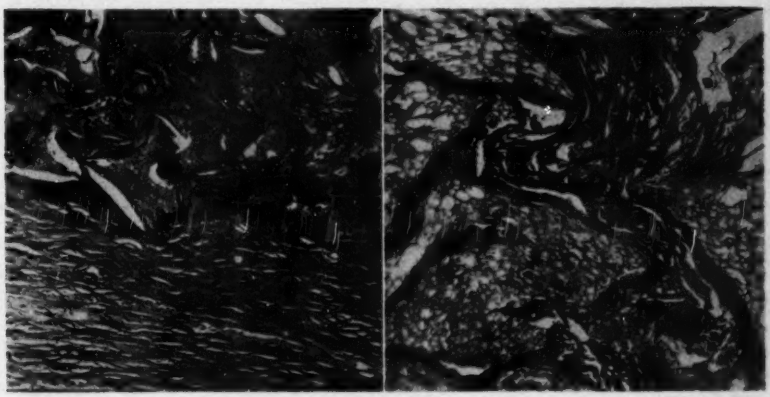

Fig. 5.—Microscopic sections through a sponge which had been implanted 12 mo. before in the breast region. Low power magnification on left and high on right. Bundles of collagen fibers, in which are a few endothelium-lined spaces, are seen between areas of sponge. The latter areas have a foamy appearance.

which were lined by what resembled a single layer of vascular endothelium. Clumps of blood cells were occasionally seen within these endothelium-lined, but seldom round or otherwise regular, channels. Occasionally, within the fibrous tissue small numbers of plasma cells or monocytes or a few lymphocytes were present.

CLINICAL STUDIES

The experimental demonstration of the unique properties of polyvinyl sponge suggested many clinical studies, several of which are in progress. For example, in selected cases large sponges have been used by Dr. O. T. Clagett to occupy dead space in the pleural cavity after pneumonectomy. The present study on the use of polyvinyl sponge to reinforce large abdominal aneurysms was begun in April, 1950.

The first patient was an elderly man with a fusiform aneurysm of the abdominal aorta. The dilatation began just below the diaphragm and ended at the bifurcation. In its central

portion the diameter of the aneurysm was estimated to be 15 cm. Duodenum was stretched over the upper right anterior and lateral surfaces, and the base of the mesentery was stretched over the midanterior surface.

Although the peritoneum was adherent to the wall of the aneurysm in several areas, which were evidently the sites of former small hemorrhages, for the most part the subserous areolar tissue could be split fairly easily by blunt dissection. A sheet of polyvinyl sponge was then placed between the aneurysm and the peritoneum in the space thus created by dissection. The sheet was stretched somewhat as it was anchored to the wall of the aneurysm with a number of interrupted sutures. After several such sheets of sponge had been placed, nearly all the anterior and lateral surfaces of the aneurysm were covered with a single thickness of polyvinyl sponge. The peritoneal layer was sutured together over the sponge. The patient's condition remained good during this relatively short operation, and his convalescence was uneventful. Because only 10 mo. have elapsed since operation, it is impossible to tell how much he has been helped.

Three more patients with large abdominal aneurysms have been treated more recently in almost the same manner, one of them by Dr. J. T. Priestley. The convalescence of these patients also, although they presented poor operative risks, was smooth.

COMMENT

The early promise which polyvinyl sponge gave in our experimental investigations has so far been fulfilled. Although long-term experiments are necessary before this material is given unqualified approval for clinical use, it would seem that certain uses are warranted. For example, use of polyvinyl sponge to reinforce the wall of huge aneurysms of the abdominal aorta as described in this preliminary report seems to us to be fully justified. No other known surgical procedure can be used in such cases. The course of the disease is well known. Our experiments indicate to us that the risk of the sponge having harmful effects is small as compared with the risk of rupture of the aneurysm. Moreover, operation was not extremely difficult and imposed no great strain on the patients. The effect on the diseased aorta, whether further dilatation occurs, how long rupture is delayed, and the type of case best suited for the procedure are matters which can be decided only after longer experience.

Our experimental studies have not answered certain questions. Whether deterioration of polyvinyl sponge will occur eventually and whether tissue within or about the sponge is more prone than other tissues to infection, infarction, invasion by neoplasm or injury by thermal or mechanical forces are questions which it is still too early to answer. On the basis of our experience up to the present time it would appear that the fibrous tissue which grows to penetrate polyvinyl sponge is not different from other, noninflammatory, fibrous tissue. It will be important to appreciate, in the clinical, surgical use of sponge, that the piece of sponge which is implanted will become a piece of fibrous tissue of the same size and shape. In other words, the implant will become less resilient and firmer.

It is not possible to explain the mechanism by which living tissue adopts polyvinyl sponge and uses it as a framework for fibrous tissue or to explain why the body does not surround the sponge by a protective barrier. Yet the peculiar affinity of polyvinyl sponge for water, which is far more than a surface affinity, and the fact that tissue cells live in a water environment, give the sponge a kinship with living tissue. Perhaps tissue fails to recognize polyvinyl sponge as a foreign body, because tissue fluids enter it. Cells follow fluid, and what was inert becomes living.

SUMMARY

Polyvinyl sponge is a lightweight, wettable, resilient material which resembles sea sponge. It is made from polyvinyl alcohol and formaldehyde by a commercial process and is available in pure form.

Polyvinyl sponge may be sterilized by boiling in water and is easily cut or molded into sheets and various shapes.

Polyvinyl sponge was implanted surgically either subcutaneously, intrapleurally, or adjacent to breast, ear cartilage, periosteum or muscle in 37 experiments involving 28 dogs. Pathologic studies of sponge and adjacent tissue were made in 24 experiments at intervals up to 18 mo.

Inflammatory reaction or evidence of deterioration of sponge has not been observed. The spaces within the sponge rapidly became occupied by noninflammatory fibrous tissue.

A thin sheet of polyvinyl sponge has been placed over the wall of large abdominal aneurysms in four patients, with the expectation that fibrous tissue which grows into the sponge will strengthen the wall of the aneurysm.

EXPERIMENTAL GASTROJEJUNAL ULCERS DUE TO ANTRUM HYPERFUNCTION

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CHICAGO

IN PREVIOUS studies from this laboratory, the antrum of the stomach in dogs was found to be the sole source of the gastric secretory excitant, gastrin, and to function as an endocrine organ. When quantitative collections of gastric juice were made in Heidenhain pouch dogs, removal of the antrum was found to reduce the secretion of gastric juice by an average of 86%.[1] A similar marked reduction in secretion from the Pavlov pouch was produced when the antrum was removed from its normal location and converted into a closed pouch and its secretions drained to the exterior by means of a cannula. When this antrum pouch was subsequently transplanted into the wall of the duodenum as a diverticulum so that it could come in contact with food, the secretion from the fundus pouch was restored to the normal level. When, however, the antrum pouch was transplanted into the wall of the colon, a persistent hypersecretion of gastric juice from the Pavlov pouch occurred, suggesting that in this location hyperfunction of the antrum was produced.[2]

It is now recognized that a hypersecretion of gastric juice occurs in most patients with duodenal ulcers, both in response to the ingestion of food, to stimulation by histamine or insulin hypoglycemia, and, more particularly, in the intervals between meals, as at night when the stomach is empty. A considerable amount of evidence has accumulated implicating this hypersecretion of gastric juice as the cause of the ulcer and the chief factor in maintaining chronicity. Clinical studies have demonstrated that the hypersecretion in patients with duodenal ulcer is almost always abolished if the vagus innervation of the stomach is completely removed, thus indicating that this hypersecretion is usually of nervous origin. It has been suggested, however, that in some cases the hypersecretion might be of antrum origin

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1. Woodward, E. R.; Bigelow, R. R., and Dragstedt, L. R.: Effect of Resection of Antrum of Stomach on Gastric Secretion in Pavlov Pouch Dogs, Am. J. Physiol. **162**:99, 1950.

2. Dragstedt, L. R.; Woodward, E. R.; Storer, E. H.; Oberhelman, H. A., Jr., and Smith, C. A.: Quantitative Studies on the Mechanism of Gastric Secretion in Health and Disease, Ann. Surg. **132**:626, 1950.

and that an attempt should be made to differentiate these cases and apply treatment appropriate to the cause of the excessive secretion. With the development of an experimental method for producing hyperfunction of the antrum in experimental animals, an opportunity was provided to determine if this antrum hyperfunction could produce ulcers in experimental animals.

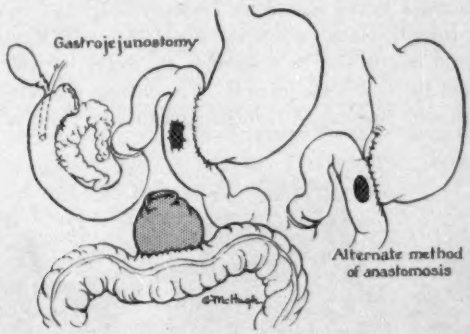

Fig. 1.—Diagram illustrating transplantation of the antrum of the stomach into the side of the colon as a diverticulum and reconstruction by end-to-side gastrojejunostomy.

Fig. 2.—Photograph illustrating multiple ulcerations in the jejunum in the neighborhood of the stoma in dog D-247 three weeks after transplantation of the antrum of the stomach into the colon as a diverticulum.

Six healthy, adult, mongrel dogs were operated on under ether anesthesia and with strict aseptic precautions. The stomach was transected at the pylorus, and a second incision was made from the lesser to the greater curvature of the stomach

about 6 cm. proximal to the pylorus. Care was taken to preserve the blood supply to the antrum, along both the lesser and the greater curvature. The lower end of the stomach and the upper end of the duodenum were infolded and closed. The proximal portion of the separated antrum was then anastomosed to the side of the transverse colon so that it projected from the colon as a diverticulum but retained its original blood supply. Intestinal continuity was reestablished by anastomosing the upper cut end of the stomach to the side of the jejunum (Fig. 1). In several animals, the stomach was partially closed so that the anastomosis with the jejunum was not more than 3 cm. in length. In the remainder, the entire cut end of the stomach was anastomosed to the side of the jejunum. The animals recovered promptly from the operation and were maintained thereafter on the stock diet of the laboratory.

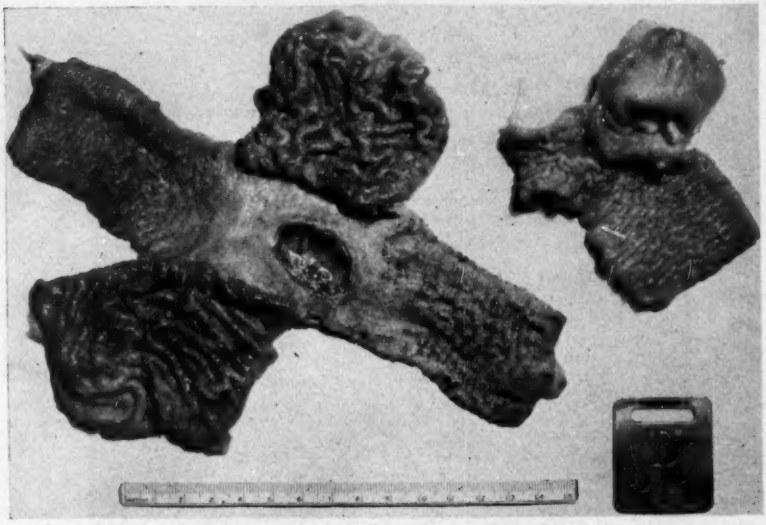

Fig. 3.—Photograph illustrating an oval jejunal ulcer near the gastroenterostomy stoma of dog D-241 in which the antrum of the stomach had been transplanted into the colon 22 days before.

For the first two weeks, all the animals appeared in excellent condition and ate their food in a normal manner. During the third week, however, three of the animals seemed to lose appetite and ate meagerly or refused food altogether. One of these animals was killed on the 21st day, and at autopsy a large ulcer was found in the jejunum approximately 1 cm. from the line of anastomosis with the stomach. In addition, there were multiple smaller ulcers occupying the first 6 to 8 in. (15 to 20 cm.) of the jejunum (Fig. 2). The large ulcer was filled with clotted blood, and tarry stools had been observed in this animal for four or five days before it was killed. The second animal was killed after 22 days, and a large, sharply punched-out ulcer, approximately 3 cm. in diameter, was found in the jejunum a short distance from the line of anastomosis with the stomach (Fig. 3). The third

animal was killed after 24 days, and in this instance also an ulcer was found in the jejunum just distal to the line of anastomosis with the stomach. In all three of these cases, the antrum transplant into the side of the colon remained viable and was filled with fecal material. The mucosa of the antrum and of the adjacent colon appeared entirely normal. No ulcers were found in this area. The fourth animal was found dead in his cage on the 35th day after the operation. At autopsy generalized peritonitis was found arising from a large perforated ulcer in the jejunum near the line of anastomosis with the stomach. This was a huge ulcer, measuring 2 by 5 cm., and almost entirely encircling the anastomosis (Fig. 4). The fifth animal remained well and in good condition, and when it was killed on the 42nd day, no ulcers were found anywhere in the gastrointestinal tract. The sixth animal remained well and in good condition until the 90th day after the operation, when it lost appetite and refused most of its food. It was killed on the 100th day, and two

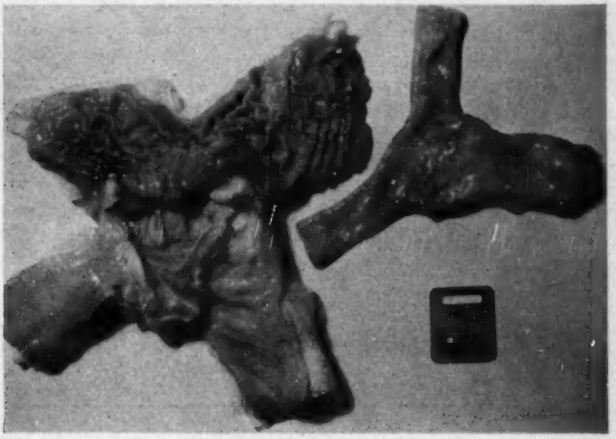

Fig. 4.—Photograph illustrating a very large perforated gastrojejunal ulcer in dog D-253, which died of generalized peritonitis 35 days after transplantation of the antrum of the stomach into the side of the colon.

large ulcers, measuring 1 by 2.5 cm., were found in the jejunum near the line of anastomosis with the stomach.

Spontaneous peptic ulcers rarely appear in the domestic dog and, in our experience, are never seen following gastroduodenostomy or gastrojejunostomy unless the alkaline secretions of the duodenum are deviated away from the region of the anastomosis or some additional experimental procedure is carried out. Montgomery [3] observed gastrojejunal ulcers when a hematoma was intentionally produced at the site of the anastomosis, but otherwise the animals remained free from lesions. The prompt appearance of large, typical, gastrojejunal ulcers in five of six animals in which an excessive secretion of gastric juice was maintained by transplantation of the antrum into the colon is thus significant and of interest in the

3. Montgomery, A. H.: Gastrojejunal Ulcer, Arch. Surg. 6:136 (Jan.) 1923.

pathogenesis of ulcer disease in general. A new method is available for the production of experimental ulcers in animals under which the nutritive state remains excellent until the lesions appear. While it may be concluded from these experiments that a hypersecretion of gastric juice with ulcer formation occurs when the antrum is hyperactive, it remains to be demonstrated whether or not this mechanism plays a role in spontaneous ulcer in human patients.

CONCLUSIONS

1. A sustained hypersecretion of gastric juice is produced in dogs by transplantation of the antrum of the stomach into the side of the colon as a diverticulum.

2. Typical, large, progressive, gastrojejunal ulcers developed in five of six animals in which the antrum was transplanted into the colon and intestinal continuity reestablished by gastrojejunostomy. These experimental ulcers displayed the characteristics of hemorrhage, progression, and perforation seen in clinical lesions.

AN EVALUATION OF FIVE YEARS' EXPERIENCE WITH VAGOTOMY IN TREATMENT OF CHRONIC PEPTIC ULCER

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IT SEEMS quite apparent that the general enthusiasm which first greeted vagotomy a few years ago has abated considerably, and that it has become definitely limited in its application in some clinics and in others has been given up altogether. Moreover, the idea has become quite prevalent that the good results that followed its use were due to the gastroenterostomy with which it was usually accompanied, inasmuch as workers showed many years ago that gastroenterostomy alone was effective in approximately 85% of patients with chronic intractable peptic ulcer of the duodenum in which some degree of obstruction was present. In general, this reaction to vagotomy was not at all surprising, because in 1945 and 1946 almost everybody seemed anxious to try out the new procedure; the cases were not too carefully selected and studied, and many times the operation was undertaken by men not too well qualified to do this type of procedure. It was inevitable, therefore, that the disappointing results which too often followed were bound to create false impressions of the true value of vagotomy as a method of surgical treatment for chronic peptic ulcer.

PREVIOUS STUDY

On Feb. 20, 1948, in an effort to define more clearly the true value of this operation, we[1] reported the results in a series of 101 patients who had been subjected to vagotomy for chronic peptic ulcer, 66 of whom were operated on at the Veterans Administration Hospital at Hines, Ill., and 35 at the Presbyterian Hospital in Chicago. The study involved the work of 18 different general surgeons, all members of the American Board of Surgery, but among them only a few had given special attention to the anatomical distribution of the vagus nerves, either in the anatomical laboratories or in the postmortem room.

For the most part, these 101 patients had had long-standing chronic peptic ulcers which, for one reason or another, had failed to respond well to a medical regimen. In more than half of them the duration was over 10 yr.; the longest was 40 yr. In 87 the lesion involved the duodenum only; in five it was situated on the

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1. Miller, E. M., and Olwin, J. H.: Results of Resection of Vagus Nerve for Chronic Peptic Ulcer, Arch. Surg. **57**:353 (Sept.) 1948.

lesser curvature of the stomach, and in eight, at the site of anastomosis after a previous gastroenterostomy or gastric resection. In 47 there had been a history of severe bleeding, often repeated several times; 26 had had perforations, and in 36 patients obstruction of some degree was demonstrable clinically or on roentgenograms. These patients represented, therefore, clinical problems in which the surgeon was justifiably called on to decide among a gastroenterostomy, a partial gastrectomy, or a resection of the vagus nerves either above or below the diaphragm. Nine of these patients at the time of this report had moved away from Chicago, could not be traced, and, therefore, were classified as "lost." That left 92 patients on whom definite information had been obtained, and upon these the study of results of treatment was based. The results were as follows: good, 76 patients (82%); fair, 13 patients (14%), and poor, 3 patients (3.2%). The conclusions reached at that time were these:

1. Vagus nerve resection in properly selected cases, and especially when combined with gastroenterostomy, has a very definite place in the surgical treatment of patients with chronic peptic ulcer whose condition has failed to respond to medical therapy.

2. In the treatment of chronic gastric ulcer vagotomy is not deemed advisable, except in the patient in poor condition with a high-lying ulcer involving the cardia or the fundus and proved to be benign by biopsy.

3. This procedure allows the surgeon the opportunity to choose between a long-established dependable operation (gastric resection) and a less hazardous and simpler procedure which, at present at least, seems to offer approximately an equal chance of favorable results.

PRESENT STUDY

After an interval of three years we are again reporting on a follow-up study of this same group of patients, with the addition of 13 new patients, all operated on by one of us (E. M. M.) during 1948, 1949, and the early months of 1950. In all 13 patients a chronic duodenal ulcer had existed for several years (40 yr. was the longest duration); six of them had had severe hemorrhages, one repeated three times; five had had perforations of the ulcer, all closed surgically; two had had previous gastroenterostomies and one a partial gastrectomy. The addition of these 13 to the original 101 made a total of 114, but during these three years a few of the nine patients originally classified as lost have been found, and a few others have gradually become lost, so that at the present writing 14 are classified as lost and an even 100 patients remain on whom this study of the results of therapy is based.

How does the picture today compare with that of three years ago? We are forced to admit that, in general, it does not appear to be as good as it was at that time. Maybe we have been too critical in our analysis; perhaps we have been too conscientious in our effort to be fair in the reclassification of these patients, but in reality our criteria have remained the same. A good result is still one in which the patient is clinically well, has no symptoms of peptic ulcer demonstrable by roentgenogram or otherwise, is able to eat a regular diet, takes no medicine, has no bleeding, is holding or gaining in weight, is able to continue at his work, and is well satisfied with his operation. A fair result is one in which the patient is

entirely relieved of symptoms of ulcer but is still bothered in some degree by minor difficulties, such as fulness after meals, frequent belching, or occasional mild episodes of diarrhea, none of which is serious enough to interfere with his occupation. A poor result exists when ulcer symptoms have definitely recurred as judged clinically or by roentgenogram, or a new ulcer has formed, or there has been a return of bleeding or of persistent diarrhea with loss of weight, and the patient is unhappy about his operation. We have learned from experience that the insulin test, while ordinarily an accurate indication of the completeness of the vagotomy, is not always reliable, because in several instances the reaction has proved to be positive in some degree when the clinical result appeared to be excellent and has been negative at times even though the patient's condition was definitely classified as poor.

Group I: Good Results.—In comparing our figures, we find that three years ago 76 (or 82%) of a total of 92 patients had good results, whereas now 71 (or 71%) of a total of 100 are in this class. This change is due to the fact that one patient has been salvaged from the lost group, one has been picked up from the poor class, two transferred from the fair category, and 13 new patients were added. On the other hand, three patients have transferred to the fair group, four have been dropped from consideration in the statistics because they could not be traced during this past year (a circumstance which seriously alters our percentage of good results), and 15 have by reevaluation been shifted from the good to the poor classification. This last change has been, on the surface at least, a severe blow and will receive some comment later on. By and large, we have been well pleased with the progress of the patients whose conditions have been classified as good, and anyone who studied carefully the detailed records of these persons would be impressed by the almost spectacular changes that have taken place in their lives, because, almost without exception, not only are they well satisfied with their operation but they are enthusiastic in their praise of their physicians and the hospital and are anxious that other persons who suffer from ulcer might have the advantages of the same type of treatment. Let us cite a typical example:

CASE 1.—Miss L., aged 50, had a history of duodenal ulcer for about 31 yr., with bleeding many times. She had gradually increasing difficulty in remaining on a medical regimen, even though she was a graduate nurse of the Presbyterian Hospital and a very intelligent woman. Roentgenologic evidence repeatedly confirmed the presence of an ulcer in the duodenum, and there had been no evidence of obstruction at the pylorus. Transthoracic vagotomy (E. M. M.) was performed Oct. 18, 1946. The postoperative course was smooth except for temporary abdominal distention and difficulty in swallowing which lasted about a week. Her postoperative course during these last four years has been almost ideal. She has had no distress of any kind, has been able to eat any kind of food, and had taken no medicine. There has never been any diarrhea; in fact, she has a tendency toward constipation. She has returned to the hospital for study on several occasions, and each time the insulin tests have given negative reactions. Her comment on Oct. 12, 1949, was this:

"Since four weeks after the operation I have never lost one hour from work or pleasure because of ulcer distress. I can always talk about my operation, and I do appreciate what the doctors did in persuading me to go through with it. I am eternally grateful and will gladly do anything I can to further the cause of vagus nerve surgery."

An analytical review of this group of 71 patients reveals some interesting facts. In 70 of them the ulcer was in the duodenum and in one on the lesser curvature of the stomach. Sixteen had had perforations (all of them closed by operation); four had had previous gastroenterostomies; four had had previous partial gastric resec-

tions, and seven had anastomotic ulcers. At the time of the vagotomy, in 16 the thoracic approach was used, and the vagus nerves were resected above the diaphragm without the addition of gastroenterostomy; in six abdominal vagotomy alone was performed, and in 49 abdominal vagotomy and gastroenterostomy were combined. As far as the postoperative insulin test was concerned, the reaction was positive in some degree for nine patients even though the clinical result was excellent.

Group II: Fair Results.—Again comparing our figures, we find that three years ago 13 (14%) of the total of 92 were in this group, whereas now there are only 8, or 8%, of the total of 100. This change has been due to the fact that three have been transferred from the good group; the conditions of two have been reclassified as good; four have been changed to the poor group, and two have been dropped from consideration because they were lost. A typical example of a patient in this group follows:

CASE 58.—Mr. Wm. W., aged 37, had a history of duodenal ulcer for more than 18 yr., with one episode of bleeding. The preoperative insulin test showed 104 units of free acid, with a total output of 116 units. Abdominal vagotomy with gastroenterostomy (W. V.) was performed on May 27, 1947. The postoperative course was fairly smooth except for some diarrhea lasting two and one-half months. The postoperative insulin test showed 16 units of free acid and a total of 30 units. A letter from the patient, dated Oct. 19, 1949, is as follows:

"The operation has helped me a great deal. I have been able to work almost all the time since August, 1947. I had diarrhea the first few months, but it has not bothered me much since then. I have not gained weight and have stayed at about the same weight since leaving the hospital. In the last six months I have been bothered some by gas and sometimes by pain, but it is not like it was before the operation."

In reviewing the records of these patients, we find that the ulcer in all instances was located in the duodenum, and in one case at the site of anastomosis following a previous resection. Two of the patients had had perforations. Abdominal vagotomy was performed without gastroenterostomy in three, and in the remaining five abdominal vagotomy and gastroenterostomy were combined.

Group III: Poor Results.—Again returning to a comparison of our figures, we find in this group a considerable discrepancy. Three years ago there were only three patients (3.2%) in this group of a total of 92. Now there are 21 patients in the group, with the amazing percentage of 21 on the basis of a total of 100. This has come about for several reasons. The first has to do with the previous classification of the patients. The condition of only two of them was previously classified as poor; four have come down from the group with fair results, chiefly because of persistent diarrhea; one was placed in the group of good results because of the entire disappearance of symptoms of what was thought for a while to be a stoma ulcer, and 15 have been dropped from the good class for a variety of reasons which warrant elucidation.

CASE 4.—Mr. J. S., aged 36, had a chronic duodenal ulcer for 18 yr. A perforation was closed in 1935. Transthoracic vagotomy (E. M. M.) was performed in 1947. The postoperative course was good until January, 1951, when routine stomach fluoroscopy suggested a mild reactivation of the duodenal ulcer.

CASE 11.—Mr. T. O., aged 44, had a chronic duodenal ulcer for 22 yr., with a perforation that was closed in 1937, at which time gastroenterostomy was performed. In 1947 roentgenologic evidence was present of stoma ulcer, from which he had been bleeding. On July 1,

1947, transthoracic vagotomy was performed (E. M. M.). The postoperative course was very good. The postoperative insulin test gave a negative reaction. The result was classified as good until Dec. 20, 1950, at which time routine stomach fluoroscopy revealed some tenderness over the midepigastrium, but no clear-cut stoma ulcer could be made out. In January, 1951, the roentgenologic evidence of a marginal ulcer was a little more definite and he was at once placed on a medical regimen, which easily controlled the situation.

CASE 27.—Mr. C. K., aged 51, had a chronic duodenal ulcer for four years with bleeding and one perforation. There was roentgenologic evidence of a slight narrowing at the duodenum. Abdominal vagotomy and gastroenterostomy (J. O. and E. M. M.) were performed Sept. 22, 1947. The postoperative course was smooth, with a negative reaction to the insulin test. The result was classified as good until about February, 1948, when stomach fluoroscopy showed evidence of a marginal ulcer, with some narrowing at the anastomosis. Acid values had returned to moderate proportions. Gastric resection has been advised, but thus far the patient has not consented to another operation.

CASE 28.—Mr. B. M., aged 50, had a chronic duodenal ulcer for three years, with no bleeding or perforation. The preoperative insulin test showed 87 units of free acid, with a total output of 103 units. Abdominal vagotomy and gastroenterostomy (J. O. and E. M. M.) were performed Oct. 27, 1947. The postoperative course was smooth, and a negative insulin reaction was obtained. The result was classified as good until February, 1948, when, being a heavy drinker, the patient returned to the Veterans Administration Hospital, Hines, Ill., for study. He died in May, 1948, and autopsy showed the presence of an active ulcer in the posterior wall of the duodenum and another one in the stomach.

CASE 95.—Mr. R. G., aged 43, had chronic duodenal ulcer for seven years, with three episodes of severe bleeding. The roentgenogram showed some degree of narrowing at the pylorus. Thoracic vagotomy was done June 10, 1947 (J. D.). The postoperative course was complicated by some degree of gastric retention and mild diarrhea. An insulin test done 10 days after operation showed 32 units of free acid and a total output of 65 units. After eight months retention had disappeared, and his condition was classified as good. He seemed well satisfied with his operation, but in February, 1951, evidence of a recurrent duodenal ulcer was found by roentgenogram, and he was placed on a medical regimen.

CASE 97.—Miss A. W., aged 48, had chronic duodenal ulcer for seven years with one episode of bleeding. No evidence of outlet obstruction was seen on the roentgenogram. Preoperative insulin studies revealed 73 units of free acid, with a total of 86; the sugar level was 40 mg. per 100 cc. Transthoracic vagotomy was performed on Feb. 11, 1946 (J. D.). The postoperative course was very smooth. She was asymptomatic for three years, and the result was classified as good. However, there was gradual development of signs of outlet narrowing. Gastric resection was done Feb. 2, 1950 (J. D. and E. M. M.). The result was excellent one year after operation.

Comment.—It seems probable that if a gastroenterostomy had been done originally at the time of vagotomy the result might have continued to be good without further surgical measures.

CASE 57.—Mr. A. G., aged 57, had a chronic duodenal ulcer for nine years with one episode of bleeding. Abdominal vagotomy and gastroenterostomy were done April 29, 1947 (W. V.). A smooth postoperative course resulted. Ten months later his condition was classified as good. In 1948 fulness, heartburn, and belching after meals developed. He returned to the hospital, and a pyloroplasty was done. He felt well for six months, only to have a recurrence of bleeding. There was never any diarrhea. He is fairly well satisfied with the operation, but he is unable to continue at work.

CASE 67.—Mr. G. F., aged 42, had a chronic duodenal ulcer for four years. Abdominal vagotomy and gastroenterostomy were done Oct. 16, 1947 (J. M.). The postoperative course was smooth except for diarrhea, which continued more or less since his operation. In October, 1949, symptoms of peptic ulcer returned, and he has been unable to continue at work.

CASE 61.—Mr. C. J. M., aged 42, had a chronic duodenal ulcer for five years. It perforated in March, 1947. Abdominal vagotomy and gastroenterostomy were done on May 21, 1947 (Dr. W.). The postoperative course was smooth except for a wound separation. The post-

operative insulin test on June 26, 1947, gave a negative reaction. The result was evaluated as good. In January, 1951, he stated that he was not free from ulcer symptoms; he had some diarrhea, was not satisfied with the operation, and was able to work only part time. He did not return to the hospital for further study to determine the cause of his symptoms.

CASE 62.—Mr. R. S., aged 39, had chronic duodenal ulcer for three years, with one episode of bleeding. Abdominal vagotomy without gastroenterostomy was performed on Aug. 1, 1947 (Dr. W.). There was a smooth postoperative course, but the reaction to the postoperative insulin test was positive. Clinical evaluation after six months was that the patient's condition was good. In a letter on Oct. 17, 1949, he wrote as follows:

"After the vagus operation I continued to have distress, requiring hospitalization and removal of the gall bladder at the Veterans Administration Hospital, Hines, Ill., in February, 1948. After eight weeks the original symptoms, vomiting and pain, persisted though I was on a very strict diet. I was unable to work because of repeated collapses on the job with severe pain. Finally, in May, 1949, the trouble was diagnosed as a blocked bowel, and I was admitted to the United States Marine Hospital in Chicago. At operation they found my stomach was enlarged to more than double the normal size. Before anything could be done about it, the ulcer perforated and I nearly died." In the fall of 1950 a gastric resection was done, and after that he seemed well for a while. The latest information comes from the Veterans Administration Hospital, Hines, Ill., in February, 1951. He recently underwent an operation there for a gastrojejunocolic fistula, at which time another resection was performed.

Comment.—It seems quite evident that the original operation of vagotomy was incomplete.

CASE 82.—Mr. C. B., aged 53, had duodenal ulcer for three years, with perforation in 1947. Abdominal vagotomy and gastroenterostomy were done Nov. 16, 1947 (Dr. W.). The postoperative course was smooth, and he was considered to have a good result until May, 1949, when he returned to the hospital for a gastric resection. After that, his condition improved and he felt well, except for distress after eating with spells of "perspiring" and a craving for oranges, at which time he was "dizzy and weak."

Comment.—The latter symptoms are possibly on the basis of hypoglycemia, a state which not infrequently develops after gastric resection.

CASE 65.—Mr. L. J. C., aged 35, had duodenal ulcer for three years, with two episodes of bleeding. Abdominal vagotomy and gastroenterostomy were done on Feb. 11, 1947 (S. L.). A smooth postoperative course resulted, and his condition was classified clinically as good a year later, in spite of a positive reaction to the insulin test. On Jan. 4, 1951, he reported:

"I am not at present free from symptoms of peptic ulcer, and I am at the same stage as before my operation. I entered the hospital at Hines, Ill., Dec. 13, 1950, with massive bleeding, requiring blood transfusions. I am not completely satisfied with the operation, nor have I been able to continue on the job."

CASE 81.—Mr. R. E. W., aged 32, had duodenal ulcer for five years with one episode of bleeding. Abdominal vagotomy and gastroenterostomy were done on Feb. 26, 1947 (Dr. L.). The postoperative course was quite good except for some diarrhea. The result was classified as good until Oct. 23, 1949, when he reported that he was not doing well. In January, 1951, he stated that he was not free from ulcer symptoms, had lost weight, and had been able to work only part time.

Comment.—This patient certainly should return to the hospital for careful study.

CASE 101.—Mr. T. S., aged 17, had duodenal ulcer for three years, with one episode of bleeding. Roentgenologic evidence of some obstruction at the outlet was present. There was 1 to 2 l. of nocturnal secretion. Abdominal vagotomy and gastroenterostomy were done April 16, 1947 (Dr. S.). A tumor of the liver was found, diagnosed by biopsy as carcinoma, and resected. The postoperative course was smooth, and frequent studies showed no free acid. The result was classified as good until Feb. 8, 1951, when the patient reported that he had done well after operation until six months previously. At that time he began to note signs of stoma ulcer. He had had considerable diarrhea and loss of weight. He returned to the hospital in November, 1950, and was carefully studied. It was decided that an ulcer had developed at the anastomosis.

When we subject the records of these 21 patients classified as having poor results to more careful scrutiny, we find that in 20 of them the ulcer was in the duodenum and in one it was on the lesser curvature of the stomach. Three also had a stoma ulcer at the site of a previous anastomosis. There had been six perforations (all of which had been closed surgically); two gastroenterostomies had been performed, and two patients had had gastric resections. In six instances vagotomy had been done through the chest without gastroenterostomy (which could well explain the poor progress in the last year); in four patients abdominal vagotomy had been done without gastroenterostomy, and in the remaining nine abdominal vagotomy and gastroenterostomy had been combined. It is interesting to note that in the postoperative period the reaction to the insulin test in seven of these patients was negative.

The results in this group naturally throw a dark cloud over the picture, and the only rational explanation we can offer is that the vagotomy was incomplete, that vagotomy was too frequently performed (10 times) without the addition of a gastroenterostomy in the presence of some degree of obstruction at the site of the ulcer, or that there was a return of function through small branches of the vagus inherent in the esophageal wall which were not noticeable at the time of operation. Still more significant as a factor may be the inexperience of the operating surgeons, and in this connection I am reminded of a statement made by H. Daintree Johnson.[2] He cites a report on a series of 215 vagotomies published by Orr and Johnson, in which it was stated that of the first 15 operations done by these authors (based on the evidence furnished by the insulin test) all were incomplete; of the first 100 operations 27 were incomplete; of the second 100 operations nine were incomplete, and of the last 50 operations none was incomplete. When we analyze the work of the 18 different surgeons who have contributed to the series on which this report is based, we find that in more than 50% of the patients with poor results vagotomies were done by surgeons whose experience with vagotomy was less than five cases, whereas the smallest numbers of poor results were obtained by those who have had a considerably larger experience. And to bring out this point even more clearly, it may be stated that the surgeon with the widest experience in this group had good results in 93% of cases, and in only 6.8% were results classed as poor.

CONCLUSIONS

As a result of this investigation, which has covered a series of approximately 100 cases over a five-year period, the following conclusions seem to be justified:

1. The evaluation of any surgical procedure is not an easy task, because some of the favorable or unfavorable complications may in some degree be attributable to other procedures done at the same time, such as gastroenterostomy in conjunction with vagotomy.

2. The wide variety of minor symptoms which in a fair percentage of instances temporarily follow resections of the vagus nerves may at times be due to other lesions in the alimentary tract or the biliary tract, and this can be determined only by most thorough and painstaking examinations.

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2. Johnson, H. D.: Vagal Resections, in Techniques in British Surgery, edited by R. Maingot, Philadelphia, W. B. Saunders Company, 1950, p. 302.

3. While we have ample proof in this series that vagotomy is sufficient in itself to provide a permanently good result (as in our Cases 1, 3, 18, 20, 31, 45, 48, 64, 69, 78, 88, 90, 103), it is our firm belief that the combination of vagotomy with a well-performed gastroenterostomy in well-chosen cases has a definite place, if performed by a competent surgeon who has spent considerable time in the anatomy laboratory and at the autopsy table familiarizing himself with the variations in the distribution of the vagus nerves.

4. Vagotomy is by no means to be considered a substitute for gastric resection, which is a well-established procedure, but it should be seriously considered as an alternative method of treatment, carrying with it certainly a lower mortality (note the fact that there have been no deaths in our series) and offering results which at the moment seem comparable with those of gastric resection. (Let it be remembered that in this series there had been six gastroenterostomies and seven resections performed previously to vagotomy, and all were associated with a stoma ulcer.)

5. Vagotomy is not considered advisable in the patient with chronic gastric ulcer unless the patient is in too poor condition to warrant resection and the lesion is lying high in the fundus or cardia and has been proved to be benign by biopsy.

6. Vagotomy is especially indicated in treatment of stoma ulcers that have followed either gastroenterostomy or gastric resection in which the element of obstruction is not a factor. It is to be especially recommended in those instances in which, because of the extreme degree of ulcerative change in the region of the first part of the duodenum, a closure of the duodenum would be unusually difficult or hazardous and, therefore, resection considered too great a risk.

DIAGNOSIS AND TREATMENT OF SUPERIOR-VENA-CAVA OBSTRUCTION

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GRADUAL obstruction of the superior vena cava produces a syndrome which is characterized by venous distention and edema of the head, neck, and upper extremities. This syndrome when fully developed is easily recognized but must be differentiated from those conditions in which there is retardation of right auricular filling, such as occurs in congestive heart failure and pericardial disease. While cardiac disease produces generalized venous hypertension, obstruction of the superior vena cava limits the increased venous pressure to the upper portion of the body. The literature on superior-vena-cava obstruction has been adequately reviewed by McIntyre and Sykes.[1] Between 1904 and 1946 these authors were able to find 145 cases verified by autopsy or surgery. The commonest causes of this syndrome in their patients were primary endothoracic malignant growths, luetic aneurysms, mediastinitis, and localized phlebitis with thrombus formation.

A brief discussion of the surgical anatomy of the superior vena cava is pertinent (Fig. 1). This vessel is approximately 7 cm. long and extends from the junction of the right and left innominate veins to the right auricle. Approximately 2 cm. of the vessel lies intrapericardially. The azygos vein enters just above the pericardial reflection. The superior vena cava lies in close relation to the trachea, the right main bronchus, the right pulmonary artery, the aorta, and the innominate artery and is separated from the right pleural space by the mediastinal pleura. The phrenic nerve courses over its right lateral surface. The peritracheal lymph nodes lie in close relation to its posterior surface, while the thymus may lie near its anterio-medial surface.

Inasmuch as the azygos vein is a major tributary of the superior vena cava, patency of this vessel must be considered in the problem of superior-vena cava obstruction and the establishment of collateral circulation. Occlusion of the azygos vein without interference of the flow of blood in the superior vena cava is well tolerated, as has been repeatedly demonstrated when this vessel has been sacrificed

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1. McIntyre, F. T., and Sykes, E. M.: Obstruction of the Superior Vena Cava: A Review of the Literature and Report of 2 Personal Cases, Ann. Int. Med. **34**:925, 1949.

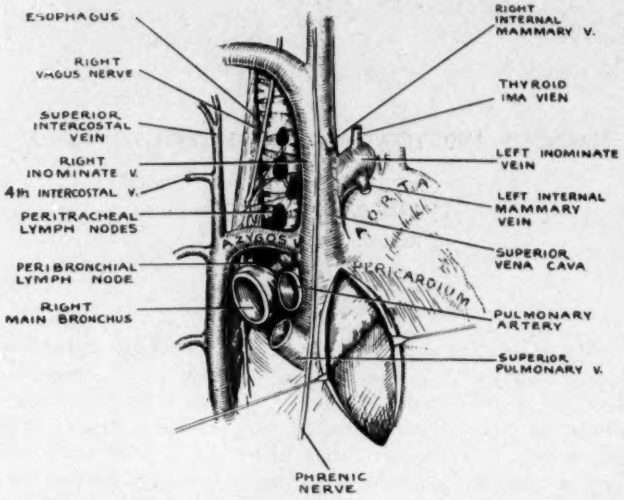

Fig. 1.—Diagram of the right mediastinum showing the superior vena cava and the adjacent structures.

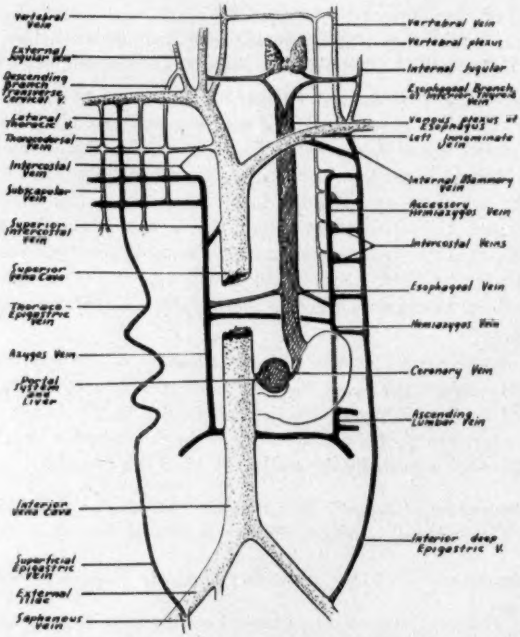

Fig. 2.—Diagram of potential collateral circulation in superior-vena-cava obstruction.

by necessity at surgery. Obstruction of the superior vena cava may occur at three points in relation to the azygos vein. First, occlusion may occur above the azygos vein with patency of this vessel and the proximal vena cava, which results in the venous return from the upper portion of the body passing by tributaries from the subclavian vein to the azygos-hemiazygos system and by these vessels to the unobstructed portion of the superior vena cava and then to the right auricle. Second, occlusion may occur at the junction of the azygos vein with the vena cava, which effectively prevents all return of blood by way of the superior vena cava, necessitating development of collateral circulation to the inferior vena cava. Under such circumstances the azygos-hemiazygos system forms an important channel with reversal of its normal flow. Third, the obstruction may occur proximal to the entrance of the azygos vein, which effectively blocks venous return to the auricle, and blood returning from the upper part of the body is shunted from the superior vena cava directly into the azygos-hemiazygos system to the inferior vena cava. As in the previous condition, there is again reversal of the direction of flow in this system. While the azygos-hemiazygos system is the major collateral pathway for the flow of blood from the superior vena cava to the inferior vena cava in this syndrome, other pathways develop, as are diagrammatically presented in Figure 2.

The location of the superior vena cava makes it particularly vulnerable to encroachment by lesions of adjacent structures. Bronchogenic carcinoma arising in the right upper lobe of the lung may directly involve the superior vena cava, while carcinoma of other portions of the lung may metastasize to the peritracheal lymph nodes, thus involving this vessel. Tuberculosis or other inflammatory lesions involving the peritracheal lymph nodes, while usually limited by the capsule, may result in adjacent mediastinitis with scarification and thrombosis of the superior vena cava and azygos veins. Lymphomas involving these lymph nodes will also produce compression of these vessels, as will aneurysmal dilatation of the adjacent arteries.

Although the diagnosis of superior-vena-cava obstruction can be made on the basis of physical examination alone, the exact location of the obstruction, the presence of collateral circulation, and the nature of the occlusive process require additional investigation. Venous-pressure determinations of both upper and lower extremities will substantiate the diagnosis, while venograms with simultaneous injection of 35 cc. of 70% iodopyracet (diodrast®) into the antecubital veins of both arms will not only demonstrate the location and degree of obstruction but also show the collateral circulation. Exploratory thoracotomy usually will be necessary to arrive at the correct pathological diagnosis.

The problem involved in the surgical treatment of superior-vena-cava obstruction is the establishment of an adequate channel for the return of venous blood from the upper part of the body to the right auricle. In 1934, Ehrlich, Ballon, and Graham [2] reported on a patient with superior-vena-cava obstruction due to Hodgkin's disease in whom marked clinical improvement resulted following surgical decompression of this vessel. Similarly, Ochsner and Dixon [3] and Gray and Skinner [4]

2. Ehrlich, W.; Ballon, H. C., and Graham, E. A.: Superior Vena Caval Obstruction with a Consideration of the Possible Relief of Symptoms by Mediastinal Decompression, J. Thoracic Surg. **3**:352, 1934.

3. Ochsner, A., and Dixon, L.: Superior Vena Caval Thrombosis, J. Thoracic Surg. **5**: 641, 1936.

4. Gray, H. K., and Skinner, I. C.: Constrictive Occlusion of the Superior Vena Cava, Surg., Gynec. & Obst. **72**:923, 1941.

reported favorable results following decompression of the superior vena cava. However, Erganian and Wade,[5] McIntyre and Sykes,[1] and Sancetta and McDonald[6] were unable to obtain favorable results by this decompression procedure. In all, nine patients have been reported in whom a surgical attempt was made to relieve the obstruction of the superior vena cava. These cases are briefly presented in Table 1.

In the past four years, 12 patients with verified superior-vena cava obstructions have been observed at the Ohio State University Hospital. Following the establishment of the diagnosis, each patient was evaluated from the standpoint of possible surgical relief of the obstruction. The case reports of these patients are presented and summarized in Table 2.

REPORT OF CASES

CASE 1.—K. L., a 36-yr.-old white laborer, was admitted to the hospital on Jan. 13, 1947, complaining of progressive fullness of his face and swelling of his arms of 10 mo. duration. He gave a history of having fallen a distance of 30 ft. while working on a lake steamer, landing on his right shoulder and face. One month following this injury he first noted an increase in the size of his face, neck, and arms.

Physical examination revealed swelling of his face, neck, and both arms and marked distention of the veins of his neck and upper extremities. Numerous subcutaneous veins were seen over the thorax and upper abdomen. Roentgenograms revealed slight widening of the upper mediastinum. The circulation time from the right arm to the tongue was 90 sec. A diagnosis of superior-vena-cava occlusion was made following venography and an interior thoracotomy performed on January 17.

Upon entering the pleural space, complete occlusion of the superior vena cava extending from the innominate veins to the auricle was demonstrated. This vessel measured 12 mm. in diameter and was filled by a hard mass firmly adherent to the wall of the vena cava. The mediastinal planes were not obliterated, and the mediastinal pleura could be dissected away from the vena cava without difficulty. The superior intercostal and the azygos veins were markedly dilated. To accomplish decompression of the superior vena cava, the mediastinal pleura was sectioned over the length of this vessel.

The patient has been observed over a period of four years. Despite the persistence of symptoms, he has been able to continue his work as a manual laborer. A venogram obtained four years following surgery again demonstrated the complete occlusion of the superior vena cava and an extensive collateral circulation predominantly by way of the azygos-hemiazygos system. The extent of the subcutaneous venous plexus at the present time is shown in Figure 3.

CASE 2.—O. S., a 56-yr.-old white housewife, was admitted to the hospital on Aug. 8, 1949, for the investigation of swelling of the face, neck, and arms. The venous pressure was found to be 180 mm. of saline in both arms and 80 mm. in the lower extremities. Electrocardiographic tracing was normal. Roentgenologic examination of the chest revealed no abnormalities; however a venogram demonstrated dilatation of the superior vena cava above an area of constriction at its midportion (Fig. 4).

A thoracotomy was performed on August 10. Exploration of the mediastinum revealed narrowing of the vena cava at the point of its entrance into the pericardium. A ringlike constriction of the pericardium was sectioned, allowing relief of the obstruction.

This patient made an uneventful recovery. Subsequent venous pressures were found to be 115 mm. of saline solution.

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5. Erganian, J., and Wade, L. J.: Chronic Fibrous Mediastinitis with Obstruction of the Superior Vena Cava, J. Thoracic Surg. **12**:275, 1942.

6. Sancetta, S. M., and McDonald, H. E.: Superior Vena Cava Obstruction Due to Chronic Mediastinitis and Phlebitis, Ohio M. J. **46**:1173, 1950.

Fig. 3.—Infrared photograph of Case 1 showing subcutaneous collateral circulation.

Fig. 4.—Venogram of Case 2 demonstrating constriction of the vena cava immediately below the visualized-right pulmonary artery.

TABLE 1.—*Surgical Treatment of Superior-Vena-Cava Obstruction (Review of Literature)*

Case	Age	Sex	Authors	Etiology	Venous Pressure in Mm. Water: Before Surgery	Venous Pressure in Mm. Water: After Surgery	Operative Findings and Procedure	Results
1	24	F	Ehrlich, Ballon and Graham [2]	Hodgkin's disease	High	Lower	V. C.* compressed by tumor; decompression	Marked improvement; died 13 mo. later of Hodgkin's disease
2	23	F	Ochsner and Dixon [3]	Traumatic thrombosis	350	278	V. C. obliterated, 5 mm. in diameter, from innominate to auricle; resection of constricting scar	Marked clinical improvement
3	37	F	Gray and Skinner [4]	Mediastinal tuberculosis	336	250	2.5 cm. mass in V. C. extending up 4.5 cm.; section of mediastinal pleura and bandlike structure	Marked clinical improvement
4	27	M	Gray and Skinner [4]	Mediastinal fibrosis	424	278	Tumor within lumen of V. C. 3 cm. longest diameter; section of band	Good functional result
5	32	M	Gray and Skinner [4]	Tuberculous lymph node	304	...	Adherent mass involving V. C.; exploratory thoracotomy	Died of hemorrhage 2d postoperative day
6	26	M	Erganian and Wade [5]	Chronic fibrous mediastinitis	290	290	Mass of fibrous tissue about V. C.; incision of mediastinal pleura	No change
7	32	M	Erganian and Wade [5]	Chronic fibrous mediastinitis	High	...	Hard mass encircling V. C.; exploratory thoracotomy	Died 1 hr. postoperatively
8	27	F	McIntyre and Sykes [1]	Chronic fibrous mediastinitis	200	350	Inflammatory mass encircling sup. V. C.; exploratory thoracotomy (Beck)	No change
9	50	M	Sancetta and McDonald [6]	Chronic fibrous mediastinitis	High	...	Superior V. C. firm and fibrotic; exploratory thoracotomy	Died shortly after operation

* V. C. stands for vena cava.

TABLE 2.—*Superior-Vena-Cava Obstruction*

Case	Age	Sex	Etiology	Venous Pressure in Mm. of Water: Before Therapy	Venous Pressure in Mm. of Water: After Therapy	Operative Findings and Procedure	Results
1	36	M	Traumatic thrombosis of superior vena cava	...	330	Occlusion of entire superior V. C.* by thrombus; section of mediastinal pleura at thoracotomy	No change over period of 4 yr.
2	56	F	Constriction of superior vena cava by pericardium	180	115	Annular constriction of superior V. C. at pericardial attachment; section of pericardium at thoracotomy	Improved
3	26	M	Lymphadenitis with adjacent mediastinitis	550	300	Complete occlusion of superior V. C. and azygos vein; shunt established by vein graft between azygos vein and intrapericardial superior V. C.	Improved
4	51	M	Bronchogenic carcinoma	...	172	Bronchoscopic biopsy of tumor of right upper lobe bronchus; x-ray therapy, aminopterin®	Improved; died 11 mo. later of metastases to liver
5	55	M	Bronchogenic carcinoma	...	...	V. C. and azygos vein occluded by tumor arising in right upper lobe bronchus; exploratory thoracotomy	Unimproved; died 10 wk. after surgery
6	42	M	Bronchogenic carcinoma	235	200	Occlusion of azygos vein and V. C. by tumor arising in right upper lobe; exploratory thoracotomy; x-ray therapy	Improved
7	43	M	Bronchogenic carcinoma	240	240	Biopsy of cervical lymph node revealed metastatic tumor; x-ray therapy	Improved
8	45	M	Neuroblastoma	410	120	Mediastinum involved by large tumor with extensive pleural implantation; exploratory thoracotomy; x-ray therapy	Improved
9	41	M	Hodgkin's disease	300	...	Axillary lymph node biopsy and bone marrow puncture; no therapy	Refused therapy; failed to return
10	59	M	Carcinoma of thymus	480	280	Tumor involvement of superior mediastinum with lateral displacement and obstruction of superior V. C.; exploratory thoracotomy; x-ray therapy	Improved; died 6 mo. later of abdominal metastases
11	28	F	Mediastinal teratoma	...	...	Tumor firmly adherent to superior V. C.; vessel displaced laterally and compressed; resection of tumor	Well
12	43	M	Syphilitic aneurysm of innominate artery	360	...	Lesion demonstrated by venograms and retrograde aortograms; antisyphilitic therapy	No change

* V. C. stands for vena cava.

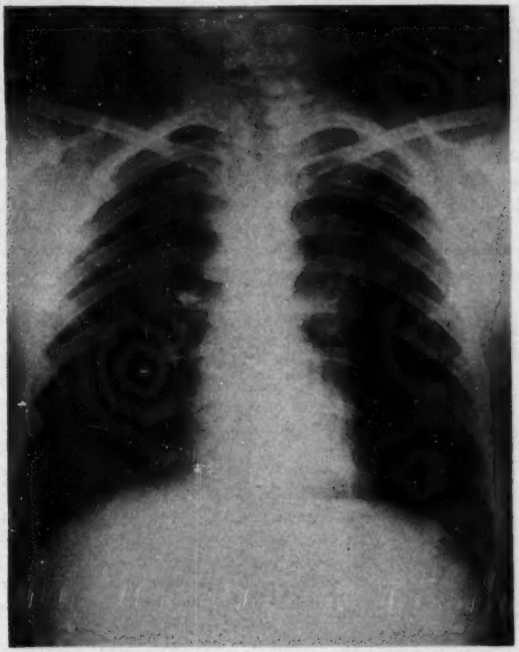

Fig. 5.—Preoperative roentgenogram of Case 3 showing the calcified lymph node in the right hilar region.

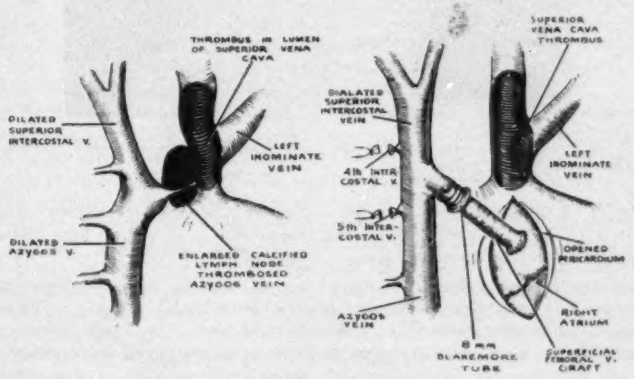

Fig. 6.—*A*, diagram of operative findings in Case 3 and *B*, method of surgical correction.

CASE 3.—R. R., a 26-yr.-old white barber, was admitted to the hospital on Jan. 14, 1950, complaining of progressive swelling and puffiness of his hands, face, and neck present over a period of two years. He had noted an increase in the size of his neck, having increased the collar size of his shirts from 15 to 16½ in one year. He was unable to follow his occupation because of substernal pain and shortness of breath. The patient's wife stated that he had shown definite personality changes, becoming irritable and restless.

On physical examination the patient was found to present the typical appearance of the superior-vena-cava syndrome. The face, neck, shoulders, and arms were puffy and edematous, and the skin had a purplish discoloration. Numerous tortuous veins were present over the shoulders, thorax, and upper abdomen. The venous pressure was 550 mm. of saline in both arms and 120 mm. in the lower extremities. The arm to lung circulation time was 13 sec. Electrocardiographic tracings showed no abnormalities. Roentgenologic examination of the chest revealed the presence of a calcified peritracheal lymph node just above the hilar region on the

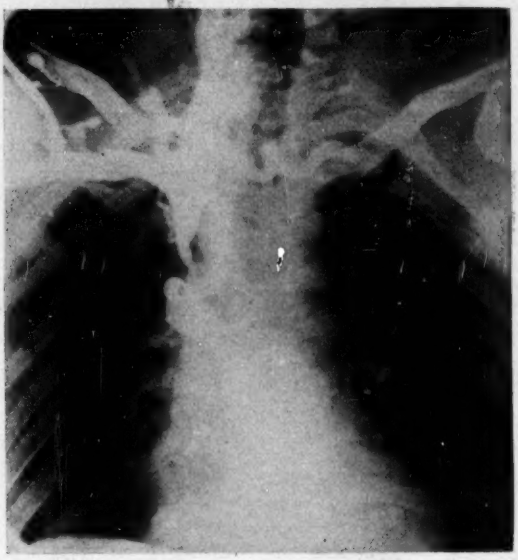

Fig. 7.—Postoperative venogram of Case 3 demonstrating the passage of contrast media through the surgically established shunt.

right (Fig. 5). A venogram showed complete occlusion of the superior vena cava. An attempt at catheterization of the superior vena cava was unsuccessful, an obstruction being demonstrated in the region of the right innominate vein.

An exploratory thoracotomy was performed on Jan. 18. This revealed complete occlusion of the azygos vein by a large anthracotic calcified lymph node. There was dense fibrous obliteration of the adjacent mediastinum, making removal of the lymph node difficult. Microscopic section showed the presence of anthracosis, calcification, and chronic inflammatory reaction. The superior vena cava was obliterated by a thrombus which extended from the midportion of the right innominate vein to the region of the pericardial reflection (Fig. 6*A*). The markedly dilated superior intercostal vein emptied into an equally dilated ascending azygos vein obviously serving as an important collateral channel for the return of blood from the upper portion of the

body. It appeared desirable at this time to divert this channel to the patent portion of the superior vena cava for a more direct return of the blood to the right auricle. Because of the presence of the right main bronchus, a direct anastomosis could not be performed without destruction of major collateral veins. It was decided to create a shunt by vein graft between the azygos vein and the patent intrapericardial portion of the superior vena cava. An 8 cm. graft was obtained from the left superficial femoral vein, and the proposed anastomosis was accomplished without difficulty as illustrated in Figure 6*B*. After the application of an obstructing clamp to the superior vena cava at the auricular junction, the graft was anastomosed to the side of the intrapericardial vena cava, using an everting continuous mattress suture of 00000 nonabsorbable surgical suture. The anastomosis of the graft to the azygos vein was accomplished by the use of an 8 mm. Blakemore tube. Upon removal of the obstructing clamp, blood was found to rush from superior intercostal and azygos veins into the right auricle.

The patient showed marked postoperative improvement. There was a decrease in the circumference of the neck from 44 cm. to 39 cm. over a period of one week, and again the patient was able to wear a size 15 collar. Venous pressure postoperatively in the upper extremities measured 300 mm. of saline solution and remained at this level at subsequent determinations. There was marked improvement in the patient's general condition, and he was able to return to his work as a barber one month following the operation. A venogram performed five months postoperatively showed extensive collateral circulation (Fig. 7), with iodopyracet entering the superior-vena-cava from the superior intercostal vein through the Blakemore tube and vein graft. The patient has continued to do well and is following his occupation.

Case 4.—H. F., a 50-yr.-old white man, was first seen on Oct. 17, 1947, complaining of puffiness of his face and swelling of his neck and arms, which had been present over a period of three months. There had been an associated dry cough with hemoptysis. On physical examination distention of the neck veins was noted and there was edema of the face, neck, and upper extremities with flushing of the face. Numerous superficial dilated veins were noted over the entire lower thorax and upper abdomen. On laryngoscopic examination paralysis of the right vocal cord was found, and on bronchoscopy a tumor was found to protrude from the bronchus of the right upper lobe of the lung which on microscopic section was found to be a squamous-cell carcinoma. Roentgenologic examination of the chest revealed an area of increased density in the right apex with tracheal deviation to the right. Venograms demonstrated complete obstruction of the superior vena cava, extensive collateral circulation along the lateral thoracic wall, and markedly dilated intercostal veins.

Because of the mediastinal invasion by malignant growth, a thoracotomy was not performed and the patient was given x-ray and 4-aminopteroylglutamic acid (aminopterin®) therapy. There was definite improvement in the symptoms with regression of the edema of the upper extremities, face, and neck. The venous pressure on completion of this therapy was 172 mm. of saline solution. Terminally congestive heart failure developed and the patient died 11 months later of congestive heart failure with evidence of extensive abdominal carcinoma metastasis.

Case 5.—K. Q., a 55-yr.-old white man, entered the hospital with a history of progressive cough and dyspnea associated with right chest pain and slight exertional dyspnea. He had noted also an increase in the size of his neck requiring a size 17 collar as compared with his normal 15. On physical examination marked fullness of the face, neck, and upper extremities was noted. The neck veins were distended, as were many small veins across the anterior chest starting just below the nipple line. Roentgenologic examination revealed a superior mediastinal tumor predominantly on the right side with tracheal compression. A venogram showed superior-vena-cava occlusion extending from the level of the right subclavian vein with evidence of collateral circulation in the region of the tumor in the upper mediastinum. Electrocardiographic tracings were normal. An exploratory thoracotomy was performed on June 11, 1949, revealing a carcinoma arising in the bronchus of the right upper lobe of the lung with invasion of the adjacent mediastinum. The peritracheal lymph nodes were markedly enlarged and were involved by the tumor. The superior vena cava and azygos veins were surrounded by the tumor. When the superior vena cava was dissected from the tumor, a thrombus was found in the azygos vein extending into the superior vena cava. Permanent section of the tumor showed it to be an undifferentiated bronchogenic carcinoma. There was no improvement in the patient's symptoms, and he died 10 weeks after surgery.

CASE 6.—C. C., a 42-yr.-old white welder, was admitted to the hospital on Aug. 13, 1950, complaining of a productive cough present over a period of six months. Physical examination showed him to be essentially normal, while roentgenologic examination of the chest showed atelectasis of the right upper lobe with increased density in the right hilum, elevation of the right side of the diaphragm, and deviation of the trachea to the right. On bronchoscopy narrowing of the bronchus of the right upper lobe of the lung with hilar fixation in this region was demonstrated; however no malignant cells could be found in the aspirated material.

An exploratory thoracotomy was performed on August 16 through a posterolateral incision. On entering the pleural space a large lobular mass was found in the hilar region with fixation of all hilar structures. There was complete occlusion of the azygos vein by the tumor, which extended to and surrounded the vena cava. The tumor also extended along the bronchus of the upper lobe of the lung into the region of the trachea. The inferior pulmonary vein was occluded by a thrombus. Biopsy showed the tumor to be an undifferentiated bronchogenic carcinoma.

Four weeks following the exploratory thoracotomy swelling of the face, neck, and arms developed and a venogram performed at this time revealed irregularity with marked narrowing of the superior vena cava just above the auricle. The azygos vein did not fill. There was marked distention of the veins in the neck and arms. The patient was given a total of 3,000 r over the superior mediastinum and right thorax with disappearance of the swelling of the face and upper extremities. Venous pressure at this time was found to be 235 mm. of saline solution. At the time of this report, six months following the thoracotomy, the patient had a slight cough; however, he showed no evidence of edema of the face or upper extremities.

CASE 7.—H. B., a 42-yr.-old white clerk, was admitted to the hospital on Jan. 25, 1951, for the investigation of pain in his right shoulder and arm present over a period of four months. Two weeks prior to admission the patient also noted hoarseness and a slight cough developed.

On physical examination enlarged, hard left supraclavicular lymph nodes were found. The veins of the neck, shoulder, and right arm were distended. Venous pressure in the right arm was 280 mm. of saline solution and in the left 150 mm., while in the lower extremities pressure was 40 mm. Roentgenologic examination revealed a right superior mediastinal mass measuring approximately 4 cm. in diameter with left displacement of the trachea. A venogram showed narrowing of the superior vena cava by an external mass.

On bronchoscopy paralysis of the right vocal cord was noted; however no tumor could be observed in the bronchus of the right upper lobe of the lung. A biopsy of a supraclavicular lymph node revealed the presence of a poorly differentiated carcinoma which on the basis of the roentgenologic findings was diagnosed as a bronchogenic carcinoma.

The patient was given x-ray therapy over a period of two weeks; however there was no change in the venous pressures of the upper extremity as demonstrated by subsequent measurements. This patient was still under observation at the time of this report.

CASE 8.—F. C., a 45-yr.-old white barber, was admitted to the hospital on Jan. 15, 1951, in acute respiratory distress. The patient had first noted a cough and pain in his right chest approximately one month previously. Two weeks prior to admission roentgenologic examination had revealed the presence of a mediastinal mass.

On physical examination complete flatness was found over the entire left thorax. Roentgenologic examination revealed a shift of the mediastinum to the right with a homogeneous density throughout the left thorax. The upper mediastinum was markedly widened and lobular masses were noted in the upper mediastinum bilaterally. Serosanguineous fluid removed from the left thorax showed the presence of anaplastic cells suggestive of malignant growth.

On January 18, an exploratory thoracotomy was performed. The mediastinum was found to be involved by a large lobular mass making identification of individual structures impossible. The pleural surface was covered with numerous soft, red tumors suggestive of malignant implants. Examination of the removed tissue showed it to be a neuroblastoma.

One week postoperatively marked swelling of the face, neck, and upper extremities developed with venous distention. Venous pressure at this time in the upper extremities was found to be 410 mm., while in the lower extremities it was 150 mm. of saline solution. A venogram was performed and revealed occlusion of the superior vena cava; however, no collateral circulation could be demonstrated. The patient was given a total of 2,000 r over the mediastinum with marked improvement in the symptoms and return of the venous pressures to 120 mm. of saline solution in two weeks.

CASE 9.—C. B., a 41-yr.-old Negro man, was admitted to the hospital on Dec. 29, 1949, complaining of a slight cough associated with swelling of his face, neck, and arms of three months' duration. On physical examination the upper half of his body was found to be edematous

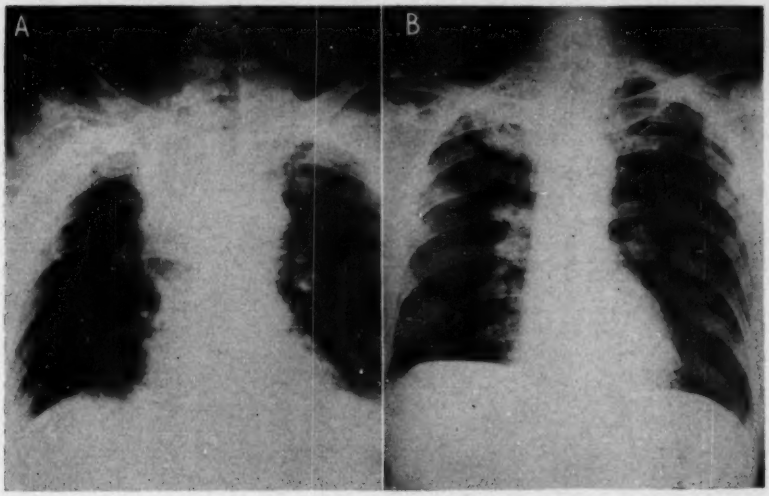

Fig. 8.—*A*, preoperative venogram of Case 10 showing compression and displacement of the superior vena cava. *B*, roentgenogram following irradiation therapy.

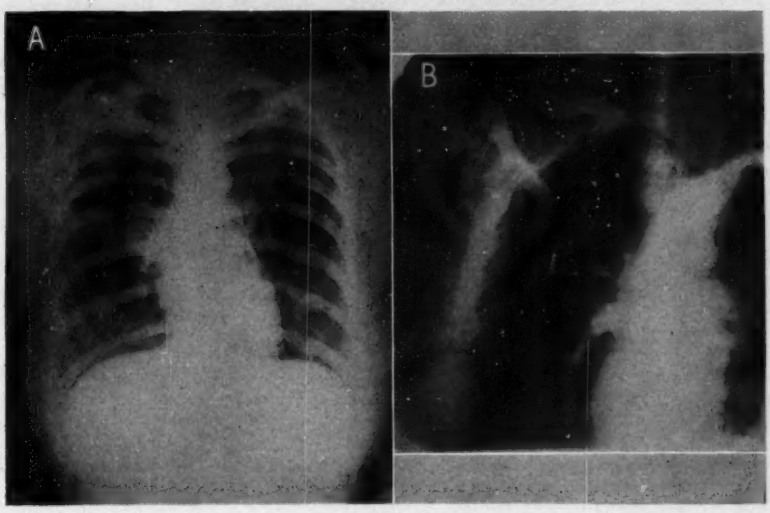

Fig. 9.—*A*, preoperative roentgenogram of Case 11 showing right hilar tumor. *B*, preoperative venogram showing vena cava compression and displacement.

and distended veins were noted over his neck and anterior chest. Roentgenologic examination showed an increase in the width of the transverse diameter of the upper mediastinum with marked enlargement of the hilar lymph nodes. A venogram showed a venous block of the

superior vena cava with collateral circulation through the superior intercostal and both the azygos and the accessory hemiazygos veins. Electrocardiographic tracings showed tachycardia but no other abnormalities.

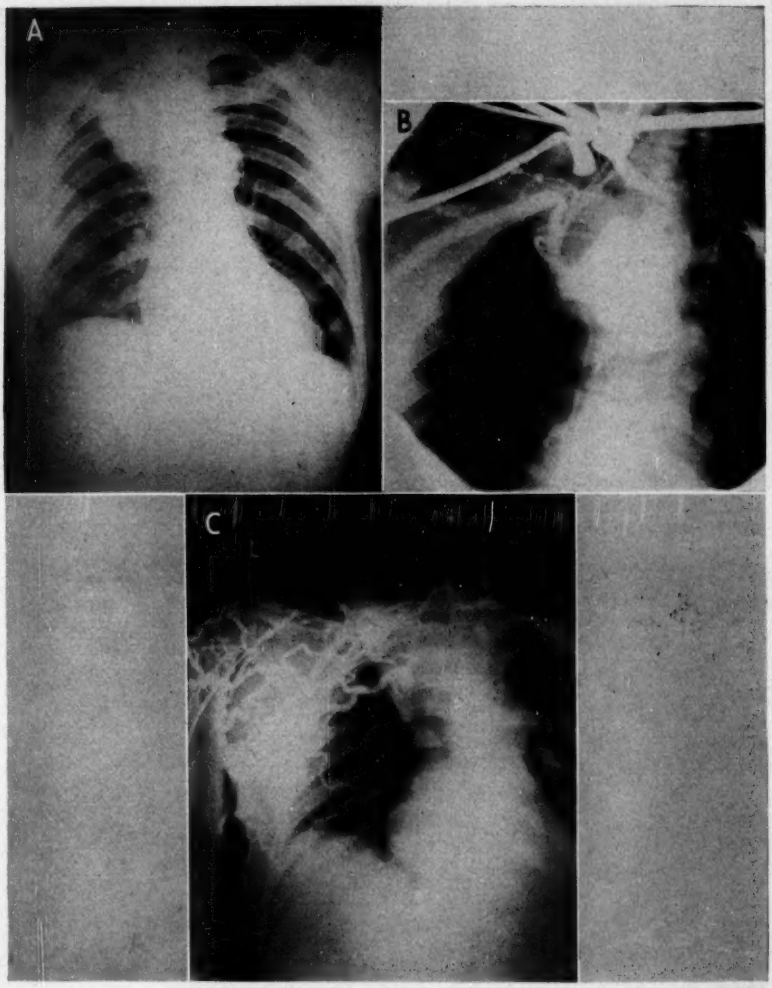

Fig. 10.—*A*, roentgenogram of chest of Case 12 showing lesion in right upper mediastinum. *B*, retrograde aortogram outlining aneurysm of the innominate artery and aorta. *C*, venogram demonstrating occlusion of the superior vena cava and collateral circulation.

On the basis of a lymph-node biopsy and bone-marrow studies a diagnosis of Hodgkin's disease was made and x-ray therapy advised. The patient refused therapy and failed to return for future observation.

CASE 10.—E. H., a 59-yr.-old white engineer, was admitted to the hospital on July 7, 1950, with the complaint of swelling of his face, neck, and arms of three months' duration. Physical examination revealed edema of his face, neck, and arms with marked distention of the veins. There were tortuous superficial veins over his lower thorax and his upper abdomen. The venous pressure in both upper extremities was 480 mm. of saline solution, while in the lower extremities it was 120 mm. Roentgenologic examination revealed an area of increased density in the right upper mediastinum, and a venogram revealed obstruction of the superior vena cava (Fig. 8*A*).

An exploratory thoracotomy was performed on August 18, at which time the upper mediastinum was found to be involved in a whitish lobular mass which completely obliterated all mediastinal structures. The subclavian vein was exposed, but the superior vena cava could not be freed from the tumor which surrounded it. The azygos vein was completely occluded. A biopsy taken of the tumor revealed it to be carcinoma of the thymus.

The patient was given a total of 4,700 r over the superior mediastinum, with disappearance of the swelling of the upper part of his body and return of venous pressure to 180 mm. of saline solution. Roentgenologic examination one month after thoracotomy revealed disappearance of the previously visualized tumor (Fig. 8*B*). The patient did well and was asymptomatic until four months after the thoracotomy, at which time there was evidence of metastasis to the liver. The patient died two months later with extensive involvement of the abdomen by metastatic tumors. There was no return of the swelling of the upper part of his body.

CASE 11.—E. G., a 28-yr.-old white housewife, was admitted to the hospital on Dec. 2, 1950. A routine roentgenologic examination four months previously had shown the presence of a mass in the right mediastinal region which on subsequent examination showed an increase in size. Physical examination showed the patient to be essentially normal. Roentgenologic studies (Fig. 9*A*) revealed a round and pulsating mass extending outward from the descending arch of the aorta and right hilar area. The tumor measured 5 cm. in diameter and projected 4 cm. into the right thorax. A venogram showed compression of the superior vena cava with displacement of the vessel to the right (Fig. 9*B*). An exploratory thoracotomy was performed on July 5. On entering the pleural space an irregular mass was found arising in the anterior mediastinum and protruding into the right thorax just above the hilus. The pedicle arose in the region of the thymus. Attempts to remove the tumor showed that it was firmly attached to the superior vena cava. A small tear was produced in the vessel during mobilization of the tumor. This tear was repaired by a running suture of 00000 nonabsorbable surgical suture with control of the hemorrhage. The microscopic diagnosis was teratoma.

CASE 12.—J. M., a 43-yr.-old Negro man, was admitted to the hospital on Nov. 12, 1950, with the complaint of hoarseness and pain in his right upper chest, neck, and shoulders of two months' duration. The essential findings on physical examination were edema of the face and neck with venous distention of the upper portion of the body. The heart was moderately enlarged to the left with a systolic murmur heard over the entire precordium and in the aortic area. The reaction to a quantitative Kahn test was positive. On roentgenologic examination (Fig. 10*A*) an area of increased density was found in the right upper chest which on fluoroscopy was found to pulsate. A retrograde arteriogram was performed with the injection of 50 cc. of 70 per cent iodopyracet into the right carotid artery. An irregular aneurysm measuring 8 by 7 cm. was demonstrated in the region of the right innominate artery and ascending aorta (Fig. 10*B*). A venogram (Fig. 10*C*) was also performed which showed complete occlusion of the superior vena cava with extensive collateral circulation.

A diagnosis of syphilitic aneurysm of the right innominate artery and ascending aorta was made. The patient was placed on antisyphilitic therapy, surgical excision of the aneurysm not being considered because of extensive involvement of the innominate artery and aorta.

COMMENT

In four patients superior-vena-cava obstruction was produced by direct extension of bronchogenic carcinoma from the right upper lobe of the lung to the adjacent mediastinum. In two of these patients (Cases 4 and 7) because of cervical metastasis and concomitant right vocal-cord paralysis thoracotomy was considered inadvisable

and irradiation therapy was given. Clinical improvement resulted in both patients; however one died 11 mo. later from extensive metastases. The second patient is still under observation.

Exploratory thoracotomy was performed in two patients (Cases 5 and 6) with bronchogenic carcinoma without evidence of distant metastasis, in whom superior-vena-cava obstruction was known to exist. This procedure was performed in an attempt to give palliative relief of the symptoms of superior-vena-cava obstruction. At the time of operation it was evident that massive invasion of the mediastinum had precluded the isolation of the superior vena cava for the purpose of decompression or any shunting procedure about the point of obstruction. Postoperative x-ray therapy in one of these patients resulted in definite palliation of the syndrome.

Cases 8 and 10 illustrate the effectiveness of adequate irradiation therapy in the relief of superior-vena-cava obstruction in the presence of highly malignant tumors. On exploratory thoracotomy in each case all mediastinal structures were found to be incorporated in a large mass of malignant growth obviating any surgical correction of this syndrome. In both patients the distressing mental and physical symptoms were promptly alleviated by irradiation therapy. In each, the venous pressure dropped markedly. One of these patients, E. H., died six months later without any recurrence of the superior-vena-cava syndrome.

Case 11, with a solitary tumor in the right hilar region, was found on venography to have compression and deviation of the superior vena cava. Considerable difficulty was encountered on operation because of the adherence of the tumor to the vessel, resulting in a tear requiring suture repair. While symptoms were not present at the time of surgery, the rapid growth of this teratoma, as proved by previous roentgenologic examinations would, in all probability, have produced clinical symptoms.

Because of the proximity of the ascending aorta and innominate artery to the vena cava, aneurysms of these structures not uncommonly produce compression of the superior vena cava as is illustrated in Case 12. Venograms and angiocardiograms of this patient demonstrated the extensive aneurysmal dilatation present and the futility of any attempt at surgical therapy.

Case 2 was referred because of superior-vena-cava syndrome. The etiology of the bandlike constriction of pericardium about the superior vena cava demonstrated both by venograms and by surgery is not clear, inasmuch as no evidence of pericardial disease was present. Nevertheless, following section of this band there was complete relief of symptoms and decrease of the venous pressure in the upper extremities.

The diagnosis of traumatic thrombosis of the superior vena cava in Case 1 was made on the basis of the history and exclusion of other etiological factors. The symptoms of superior-vena-cava obstruction appeared one month after a severe trauma to the face and right shoulder. At operation eight months later the vena cava was found to be thrombosed throughout its length without any evidence of adjacent mediastinal disease. Because of extension of the thrombus into the right auricle and its firm adherence to the vessel wall, neither removal of the thrombus nor formation of a venous shunt were applicable in this case. Mediastinal decompression did not produce any alleviation of the patient's symptoms. Venography

performed four years later did not reveal any evidence of recannulization or resolution of the thrombus. However, this patient is able to continue his regular duties as a laborer. The extent of his cutaneous collateral circulation is illustrated by a recent infrared photograph.

Case 3 presented a problem in therapy because of rapid progression of physical and mental symptoms and complete incapacitation. Complete obstruction of the superior vena cava was demonstrated by venograms and attempted catheterization. Roentgenograms demonstrated the presence of a calcified peritracheal lymph node in the region of this vessel. At thoracotomy this lymph node was found to lie medial to the azygos vein and in close proximity to the vena cava. The adjacent mediastinitis extended to the region of the innominate veins. Removal of the lymph node revealed destruction of the proximal portion of the azygos vein. The intrapericardial portion of the superior vena cava was found to be free of thrombosis and could be utilized for a shunting procedure. Both the superior intercostal veins and the remaining azygos vein were of large caliber, apparently constituting a major collateral pathway for venous return. The position of the right main bronchus precluded a side-to-side anastomosis of the azygos vein to the superior vena cava; also, it appeared impractical in this case to establish the continuity of the superior vena cava about the thrombosis by vein graft because of the involvement of the innominate veins by the thrombus. A vein graft was placed between the azygos vein and the intrapericardial portion of the superior vena cava. The patient's symptoms were relieved following this procedure. Venograms six months postoperatively demonstrated the patency of the shunt and indicated the return of blood from the upper extremities to the right auricle by this newly formed channel.

SUMMARY

A series of 12 patients with superior-vena-cava obstruction is presented to illustrate the etiology of the lesions, diagnosis, and therapy.

In six patients with primary endothoracic malignant growth, surgical therapy was inapplicable because of extensive invasion of mediastinal structures. Palliative relief was obtained in five of these patients by x-ray therapy.

Mediastinal decompression of the vena cava in a patient with traumatic thrombosis produced no clinical improvement.

Compression of the superior vena cava by a pericardial band was relieved by section of the pericardium, while compression by a teratoma was alleviated by excision of this tumor.

In one patient a vein graft was used to create a shunt between the azygos vein and the intrapericardial vena cava. Patency of this anastomosis was proved by venograms.

PULMONARY RESECTIONS FOR METASTATIC LESIONS

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THE RENEWED interest in the controversial subject of excision of pulmonary metastatic lesions has prompted us to report nine additional cases and to give our experience in selecting and handling them. The hopelessness in the prognosis for patients in whom pulmonary metastatic lesions are found, even though the primary extrapulmonary malignant growth has been totally removed, has brought about many attempts at surgical removal of the metastatic lesion or lesions and some successes. We shall try to demonstrate that the low mortality and the increased safety of pulmonary resection as practiced today justify a more radical approach to occasional surgical resection of metastatic malignant tissue.

There have been previous case reports by others, and reviews by Seiler, Clagett and McDonald [1] and by Eschappase [2] have recently been published.

The presence of a lung lesion either as a peripheral parenchymal mass or as evidenced by involvement of a major bronchus, with atelectasis and other pulmonary symptoms, makes it often impossible to state whether or not one is dealing with a primary neoplastic growth or if the lesion is on a metastatic basis. The extremely rich capillary bed of the lung parenchyma, however, constitutes a reservoir for localization of malignant emboli, and they are therefore generally multiple. As a rule, multiple metastases in the lung parenchyma can be demonstrated early and are easily diagnosed, especially if there is knowledge of a preexisting lesion of extrapulmonary origin. This fact makes the presence of larger solitary metastatic lesions more significant.

Solitary metastatic lesions in the lung may make their appearance months or years after complete removal of the primary extrapulmonary tumor. Occasionally patients are seen in whom solitary metastatic pulmonary lesions are present at the time the primary lesion is diagnosed. They may remain solitary and unchanging in size for a considerable time. The patients may or may not have symptoms referable to the metastatic pulmonary lesion, depending on the size and location. The advisability of surgical extirpation of the primary lesion along with the metastatic lesion may constitute a complex problem.

Read at the Eighth Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

From the Department of Surgery, Division of Thoracic Surgery, State University of Iowa College of Medicine.

1. Seiler, H. H.; Clagett, O. T., and McDonald, J. R.: Pulmonary Resections for Metastatic Malignant Lesions, J. Thoracic Surg. **19**:655, 1950.

2. Eschapasse, H.: Le traitement chirurgical du cancer secondaire du poumon, Toulouse, Imprimerie Toulousaine, 1950.

Among the functions of a surgeon is his responsibility toward the patient to relieve discomfort and pain and to prolong the patient's life. If the extirpation of a metastatic focus will bring about such relief of pain and even carry with it the rare possibility of apparent clinical cure, such a procedure may be highly desirable. This is particularly true if it can be done safely, without great mutilation and without considerable hazard.

The indications for selection of patients in this series were (1) the apparently complete removal of the primary neoplasm without evidence of local recurrence, (2) absence of demonstrable metastases to other organs of the body, and (3) reasonable assurance that all metastases were located in one area, making surgical resection of that area possible.

REPORT OF CASES

CASE 1.—L. B., a 50-yr.-old white woman, was first seen on Aug. 16, 1937, at which time the diagnosis of an adenocarcinoma in the cervix was made. She had had vaginal bleeding and vaginal discharge for the previous three months. Examination showed a mass of tissue which replaced the entire cervix, measuring about 3 cm. in diameter. A biopsy proved it to be an adenocarcinoma. She was treated with a course of high voltage roentgen-ray therapy and local radium application. Follow-up examination during December 1937 revealed an essentially normal pelvis. She was again seen on Dec. 30, 1946, at which time she complained of a weight loss of 40 lb. (18 kg.) and cough for six months. A roentgenogram of the chest showed collapse of the anterior segment of the right lower lobe. There was no history of hemoptysis or of shortness of breath. There was evidence of clubbing of the fingers and of hypertrophic pulmonary osteoarthropathy. On bronchoscopy a granular mass was present in the right lower lobe bronchus, occluding the entire orifice. Bronchoscopic biopsies revealed well differentiated adenocarcinoma. A comparison between the bronchoscopic biopsy and the cervical biopsy made 10 yr. previously revealed the same histologic pattern, and it was felt that the pulmonary lesion was a metastatic carcinoma and not a primary bronchogenic neoplasm.

On Jan. 24, 1947, pneumonectomy was carried out which was technically difficult. The right lung was removed, and the pathologic specimen revealed an adenocarcinoma in the lung, with some squamous metaplasia. The patient died six hours after completion of the operative procedure, and no postmortem examination could be obtained. At the time of pneumonectomy numerous lymph nodes were found which on pathologic sections proved to be replaced by adenocarcinoma.

CASE 2.—L. G. H., a white girl, was first seen at the University of Iowa Hospitals on Feb. 5, 1946, at the age of 13 yr. She complained of bilateral masses in the cervical region, deafness of the right ear and weight loss of six months' duration. Examination revealed a mass in the nasopharynx, which was biopsied and proved to be an anaplastic epidermoid carcinoma with metastasis to the cervical lymph nodes. Intensive high voltage roentgen ray therapy was given, and it resulted in disappearance of the lesion in the nasopharynx and of the metastatic lesion in the neck. The patient was followed in the Tumor Clinic at two-month intervals until February 1948. At that time she was seven months pregnant. A roentgenogram of the chest showed a solitary, sharply circumscribed lesion in the left lower lung field. The pregnancy was carried to term and was uneventful. Examination of the nasopharynx showed no evidence of recurrence of the nasopharyngeal carcinoma. Bronchoscopy yielded normal results. Bronchograms revealed the lesion to be located in the lingular segment of the left upper lobe, and it was felt that this lesion was metastatic in nature.

On April 12, 1948, lingulectomy and resection of part of the diaphragm which was involved by the tumor were carried out. The pathology report was anaplastic epidermoid carcinoma in the lingula of the left lung and the diaphragm, probably metastatic from the nasopharynx. The postoperative course was uneventful. In December, 1948, a mass developed in the upper mediastinum and over the sternum, which responded rapidly to irradiation therapy. Progressive pulmonary osteoarthropathy of the fingers also developed. The patient again became pregnant, and she was delivered of a full-term infant in April 1950. During the latter part of this pregnancy the mediastinal masses enlarged rapidly. The patient's last admission was on April 21,

1950, two weeks post partum, at which time she complained of severe chest pain, dyspnea and mild hemoptysis. The diagnosis of widespread metastatic carcinoma secondary to an epidermoid carcinoma of the nasopharynx was made. The patient died on April 28, 1950. The postmortem examination revealed no evidence of local recurrence of the epidermoid carcinoma of the nasopharynx but widespread metastasis to the lung and the hilar region, with invasion of the right main bronchus.

Case 3.—W. E., a 63-yr.-old white man, was first seen on Sept. 13, 1948, in the department of otolaryngology with the complaint of swelling of his nose. For three years he had difficulty breathing through the right nostril, with intermittent epistaxis. Examination revealed the presence of a tumor over the lateral wall of the right nasal fossa. A biopsy of this tumor proved it to be malignant melanoma. Roentgenograms of the patient's chest at this time revealed no evidence of pulmonary metastasis. There was no evidence of any regional lymph node involvement or of metastatic spread. Roentgenograms of the skull were negative.

On October 4 a radical resection of the malignant tumor was carried out, with ligation of the right external carotid artery. After the operative procedure the patient got along well, and

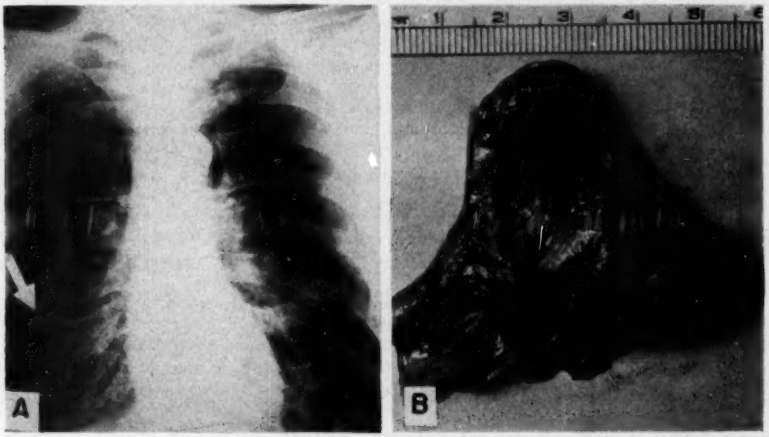

Fig. 1 (Case 3).—*A*, roentgenogram of chest showing solitary metastasis in right middle lobe; *B*, resected specimen showing solitary metastatic nodule, a malignant melanoma.

he was seen frequently in the tumor clinic of the otolaryngology department. In January, 1950, a follow-up roentgenogram of the patient's chest revealed a solitary small rounded mass in the right midlung field. Bronchoscopy revealed nothing abnormal. Bronchograms were made and the lesion found to be in the right middle lobe. The electroencephalographic studies and a lumbar puncture showed normal results. There was no evidence of any abnormality on neurologic examination. A 24-hr. urine specimen examined for melanin revealed 84 mg., which was within normal limits. Roentgenograms of the skull were normal. There was no enlargement of the liver. On February 8 a right exploratory thoracotomy, with segmental resection of the solitary metastatic lesion, was carried out. Exploration of the lung parenchyma as well as of the hilus and the mediastinum revealed no evidence of any other metastatic lesions. On pathologic examination of the specimen removed, malignant melanoma was apparent. The postoperative course of this patient was entirely uneventful. He has been seen repeatedly, and no evidence of further metastasis or of pulmonary involvement could be demonstrated. He is alive and apparently well at the present time, one year after excision of the pulmonary metastatic lesion.

Case 4.—C. S., a 60-yr.-old white man, was first seen in the department of urology with the complaint of having had hematuria since March 1944. He was admitted on April 4, 1945, and the diagnosis of a transitional-cell carcinoma of the bladder was made. Transurethral

resection of the tumor was carried out. Microscopic examination of the tissue removed showed it to be transitional-cell carcinoma of the bladder. The patient had local recurrence of the tumor in June 1945 and April 1949. In each instance it was resected transurethrally. The last fulguration for a small recurrence was in December 1949. On December 24 roentgenologic examination of the chest revealed a small peripheral round shadow in the right upper lung, which slowly enlarged during an observation period until May 1950. A cough also developed, and a roentgenogram of the chest showed a peripheral, solitary, excavated lesion. The diagnosis of a metastatic solitary lesion in the right upper lung field was made. Cystoscopy in May of 1950 revealed no recurrence of the bladder tumor.

The patient was admitted to the surgical service on May 7 for excision of the metastatic lesion, carried out on May 11. It was found that he had hilar lymph node metastases, necessitating a pneumonectomy to permit adequate regional lymph node resection. Microscopic examination of the specimen removed showed carcinoma in the lung and the bronchial lymph nodes, probably metastatic from transitional-cell carcinoma of the bladder. The postoperative course was uneventful. He made satisfactory progress until October 1950, when he again complained of some shortness of breath. Roentgenograms of the chest revealed what was thought to be lymphogenous spread of neoplasm in the left lung field.

CASE 5.—F. C., a 70-yr.-old priest, underwent partial gastrectomy for a sessile type of ulcerating adenocarcinoma with peritoneal involvement and involvement of one regional lymph node on Aug. 15, 1944. He was completely asymptomatic after the gastric resection. A roentgenogram of the chest in January, 1948, revealed a small peripheral lesion, measuring 1.5 cm. in diameter, located in the region of the left upper lobe. The patient was seen at the University Hospitals for the first time on May 28, 1950, complaining of increased fatigue. Roentgenologic examination of the gastrointestinal tract and general physical examination revealed no evidence of any local recurrence of the gastric neoplasm. In the roentgenogram of the chest a large peripheral solitary mass was visible in the left upper lobe. Bronchoscopy revealed nothing abnormal. Cytologic studies from the sputum and bronchial aspirations were negative for abnormal cells.

A left thoracotomy was carried out on June 2, 1950, and a left upper lobectomy was done. The histologic examination of the specimen removed showed a moderately well differentiated adenocarcinoma without evidence of hilar lymph node involvement. When last seen the patient was alive and well, without evidence of recurrence eight months after the pulmonary resection and nearly seven years after gastric resection for the carcinoma of the stomach.

CASE 6.—E. M., a 56-yr.-old white woman, was first seen at the University Hospitals during February 1945. She complained of rectal bleeding of three months' duration. On physical examination two polypoid lesions were found. One small polyp was 12 cm. from the anus on the posterior sigmoidal wall, and about 2 cm. above it a larger ulcerated polyp was visualized. The smaller polyp was removed through the rectum on February 23. On March 8 the sigmoid colon was resected and an end-to-end anastomosis carried out. The microscopic picture showed adenocarcinoma. No involved regional lymph nodes were present. Postoperatively a pelvic abscess developed which necessitated drainage, followed by rapid recovery. The patient was seen for follow-up examination in May 1946. She had gained 20 lb. (9 kg.) and had no gastrointestinal or pulmonary symptoms. A barium enema showed no evidence of polypi. The patient was again admitted to the Surgical Service on July 26, 1950, stating that she was well until March 1949. Pneumonia developed, and since then cough had persisted intermittently. In March 1950 she had a recurrence of the pneumonia, with increased cough. About two months before her admission the cough became productive and 10 days before admission hemoptysis occurred. There had been a weight loss of about 40 lbs. (18 kg.) during the preceding year. Roentgenograms again showed a normal colon. Roentgenograms of the chest revealed a large solitary mass located in the right lower lung field. Bronchoscopy revealed a granular mass in the region of the right lower lobe bronchus. Cytologic examination of the bronchial aspirations revealed abnormal cells.

On August 1 a right pneumonectomy was carried out. At the time of operation there was no evidence of involvement of regional nodes. The neoplasm had extended across the fissures into the middle and upper lobes. Microscopic examination of the specimen revealed adenocarcinoma similar to that seen in the previous lesion in the sigmoid colon, without evidence

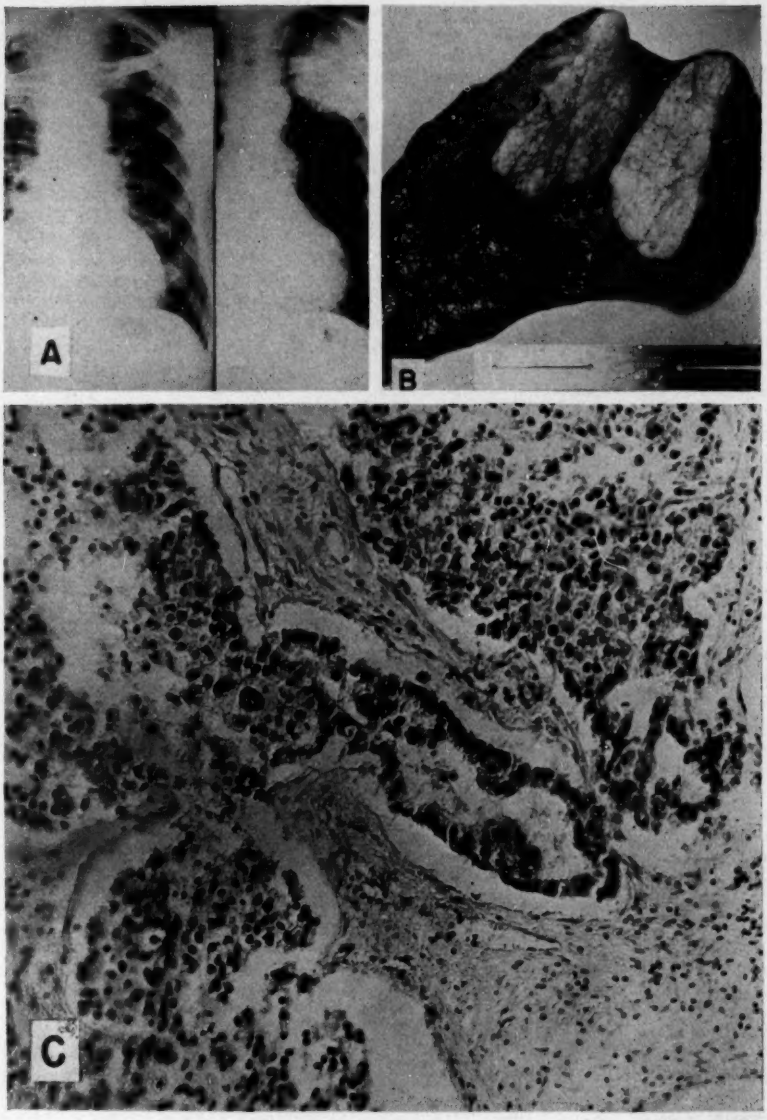

Fig. 2 (Case 5).—*A*, roentgenogram showing increase of the solitary metastatic lesion in the left upper lobe between January 1948 and May 1950; *B*, resected gross specimen, left upper lobe; *C*, photomicrograph showing metastatic adenocarcinoma of stomach in lung.

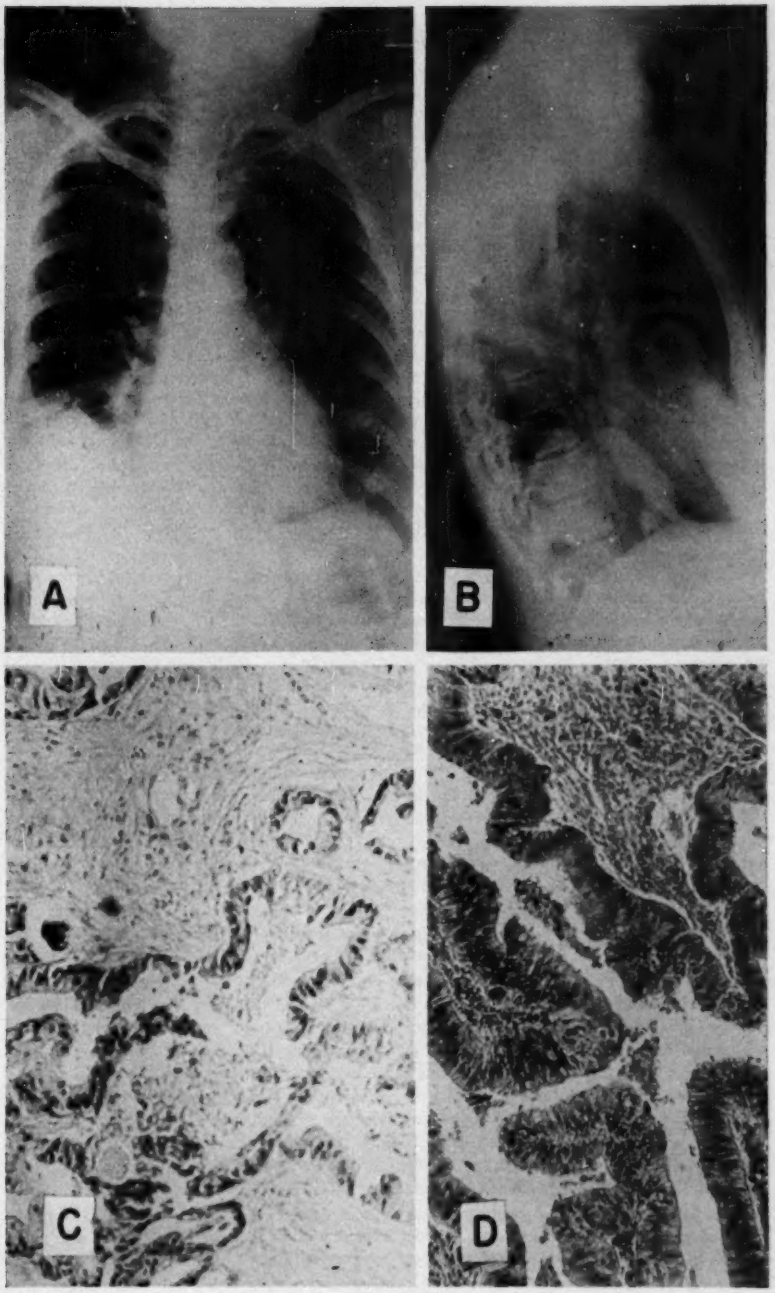

Fig. 3 (Case 6).—*A* and *B*, preoperative roentgenograms demonstrating large solitary metastasis in the right lower lobe; *C*, photomicrograph of the adenocarcinoma of sigmoid colon resected in March 1945; *D*, photomicrograph of the metastatic adenocarcinoma in lung.

of regional lymph node metastasis. The postoperative course after the pneumonectomy was uneventful, and the patient is alive and apparently well at the present time, nine months after removal of the metastasis and six years after the original resection of the colon.

CASE 7.—E. S., a 34-yr.-old white woman, was seen for the first time in the department of medicine at the University Hospitals on July 25, 1950. Her complaints were severe swelling and pain in all extremities of six months' duration. The past history revealed the fact that during August 1946 a hysterectomy had been performed for leiomyomas of the uterus. At the time of examination of the specimen an area of sarcomatous change was noted in one of the uterine myomas. Her present illness started in January 1950, at which time her left leg suddenly began to swell. Shortly afterward there was swelling of the other leg and of both hands and arms, including the elbows and shoulders. The swelling in the extremities became so painful and so severe that the patient had been confined to bed for the last three months. At the time of her admission a roentgenogram of the chest revealed a huge mass involving most of the left lung field and a solitary smaller metastatic round lesion in the right midlung field. Roentgenograms of the arms and legs showed far-advanced pulmonary osteoarthropathy, with extensive periosteal changes. The patient received a course of cortisone therapy for 14 days, 100 mg. of the drug being administered daily, without relief of symptoms. Pelvic and abdominal examination showed no evidence of local or abdominal metastasis. Bronchoscopy revealed distortion of the left lower lobe bronchus. Examinations of the sputum showed no abnormal cells. It was felt that the severe pulmonary osteoarthropathy was undoubtedly secondary to the metastatic neoplasm, and for this reason it was decided to attempt a resection of the huge mass in the left side of the chest or to obtain a biopsy for histopathologic diagnosis.

On August 22 a left exploratory thoracotomy was carried out, and a huge solitary metastatic lesion located in the lingular segment of the left upper lobe was resected. The postoperative course was remarkable. The pulmonary osteoarthropathy, which was acute up to that time, improved, and the patient was able to move the larger joints as well as the fingers within 48 hr. after the operative procedure. Microscopic examination of the specimen removed showed anaplastic cellular sarcoma consistent with metastatic leiomyosarcoma from the uterus. On the third postoperative day the patient was able to walk, which she had not been able to do for the previous three months. She was discharged on September 2 and was readmitted on October 5. Reevaluation at that time showed the left side of the chest to be perfectly clear, without evidence of recurrence of neoplasm. The solitary mass in the right midlung field was still present, and on October 10 a metastatic lesion located in the axillary segment of the right upper lobe was removed by wedge resection. The postoperative course again was uneventful. The histologic examination of the specimen removed showed a poorly differentiated leiomyosarcoma. The patient since that time has been perfectly asymptomatic and appears well six months after removal of the first metastatic lesion and four and a half years after the original hysterectomy. There is no evidence at the present time of recurrence of the neoplasm. The pulmonary osteoarthropathy has completely subsided, and the patient is doing routine work without difficulty.

CASE 8.—E. C., a 33-yr.-old white woman, noticed a mass in the outer upper quadrant of her right breast in October 1948. She was nursing a baby at that time. In December 1948 she underwent a right radical mastectomy, followed by intensive high voltage roentgen therapy to the axillary and anterior breast regions. During January 1949 a sterilization dose of such irradiation was applied to the anterior and posterior regions of the pelvis. In February 1950 cough and a tight feeling in the right side of the chest developed. The patient was seen by her local physician, who thought that she had a pneumonic episode, and she was treated with antibiotics. The same episode repeated itself in August 1950, but at this time a mass was visualized roentgenographically in the right lower lung field. She denied any hemoptysis. There had been a 20 lb. (9 kg.) weight loss in six months.

The patient was admitted to the Surgical Service on Sept. 18, 1950. Physical examination revealed a radical mastectomy scar, without evidence of local recurrence. There was some dulness in the right lower region of the chest. Roentgenograms of the chest revealed atelectasis of the right lower and middle lobes, with compensatory emphysema of the right upper lobe. Bronchograms revealed complete occlusion of the bronchus just below the right upper lobe

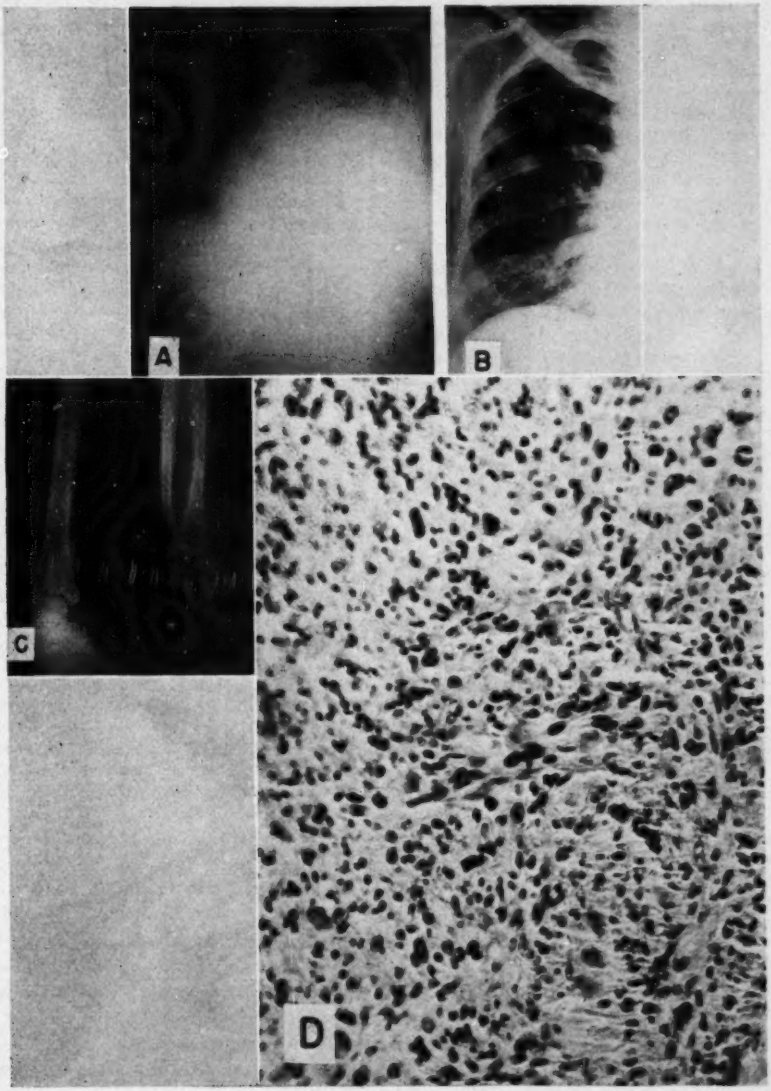

Fig. 4 (Case 7).—*A*, huge metastasis in the lingula of left upper lobe filling most of left hemithorax; *B*, smaller metastatic nodule in right midlung field; *C*, roentgenograms of forearm and distal part of leg demonstrating the periosteal changes of pulmonary osteoarthropathy; *D*, photomicrograph of the metastatic lesion in the lingula, leiomyosarcoma.

Data on Nine Cases of Resection for Metastatic Lesions

Case	Age	Sex	Primary Neoplasm			Pulmonary Metastases					Recurrence and Site	Survival
			Site	Type	Date Resected	Site	Date of Resection	Type of Resection	Hilar Node Involvement	Bronchus Invasion		
1	50	F	Cervix	Adenocarcinoma	8/16/37 X-ray therapy	Right lower lobe	1/24/47	Pneumonectomy	Positive	Right lower lobe	.....	Deceased 6 hr. after operation
2	16	F	Naso-pharynx	Epidermoid carcinoma	X-ray therapy, March '46	Lingula and diaphragm	4/12/48	Lingulectomy; resection of diaphragm	Negative	Negative	December, 1948, mediastinal mass September, 1949, supraclavicular nodes February, 1950, (pregnant) widespread metastasis	Deceased, 4/28/50
3	63	M	Nasal fossa	Malignant melanoma	10/ 4/48	Right middle lobe	2/ 8/50	Wedge resection	Negative	Negative	None	Alive
4	60	M	Bladder	Transitional-cell carcinoma	4/ 4/45	Right upper lobe	5/11/50	Pneumonectomy	Positive	Negative	October, 1950, questionable lymphogenous spread, left lung	Alive
5	70	M	Stomach	Adenocarcinoma	8/15/44	Left upper lobe	6/ 2/50	Lobectomy	Negative	Negative	None	Alive
6	56	F	Sigmoid colon	Adenocarcinoma	3/ 8/45	Right lower lobe	8/ 1/50	Pneumonectomy	Negative	Right lower lobe	None	Alive
7	34	F	Uterus	Leiomyosarcoma	August, 1946	Lingula, left upper lobe	8/22/50	Lingulectomy	Negative	Negative	None	Alive
						Axillary segment, right upper lobe	10/10/50	Wedge resection	.....	.....		
8	33	F	Breast	Adenocarcinoma	December, 1948	Right lower lung field	9/21/50	Pneumonectomy	Positive	Right intermediate bronchus	December, 1950, superior-vena cava-obstruction	Alive
9	38	M	Testis	Teratocarcinoma	1/22/50	Left lower lobe	11/ 2/50	Wedge resection	Negative	Negative	None	Alive

orifice. During bronchoscopy a lesion in the right intermediate bronchus was seen. In view of the removal of the highly malignant carcinoma of the right breast it was felt that we were dealing with a metastatic lesion in the right lung, with extension to the hilar lymph nodes and secondary invasion into the right intermediate bronchus.

On September 21 a right pneumonectomy, with extensive hilar lymph node resection, was carried out. Microscopic examination of the tissue removed revealed adenocarcinoma, poorly differentiated, in the lung, with bronchial obstruction and metastasis to the hilar lymph nodes. The patient had an uneventful postoperative course and showed marked improvement. She returned to the surgical service on December 9 complaining of shortness of breath of two weeks' duration, swelling of the neck and arms for 10 days, and weakness and loss of appetite for three weeks. Examination revealed all the signs of superior-vena-cava obstruction, which was felt to be on the basis of recurrence of neoplasm in the mediastinum. A roentgenogram of the chest showed some shift of the mediastinal structures to the right, with a normal left lung field. The patient was treated with a course of nitrogen mustard, a total of 25.6 mg. being given. This treatment was followed by rather remarkable improvement and regression of the superior-vena-cava obstruction. The patient is alive and active at the present time, five months after the pulmonary resection.

CASE 9.—H. S., a 37-yr.-old white man, was first seen at the University Hospitals on Jan. 21, 1950. He gave a history of having received trauma to the scrotum three months previous to his admission, which resulted in swelling and tenderness. The swelling decreased somewhat, but shortly before his admission the right testicle began to enlarge. On examination a nontender mass which felt firm and measured 10 by 5 cm. was palpable in the testicle. Further physical examination revealed nothing abnormal. There were no palpable abdominal masses or enlarged glands. A roentgenogram of the chest revealed a single metastatic lesion in the left lower lung field.

Orchidectomy on the right was carried out on January 23. The histologic examination of the specimen revealed teratocarcinoma with chorioepitheliomatous elements. The operation was followed by an intensive course of high voltage roentgen therapy to the mediastinal and abdominal regions and to each supraclavicular area. Also, treatment directed toward the metastatic nodule in the left lower lung field was given. The patient was again seen during June 1950, at which time he had gained weight and felt generally well. He again returned in November 1950. A roentgenogram of the chest revealed the same solitary metastatic lesion to be present in the peripheral left lower lung field. There was no other evidence of metastasis on physical examination. On November 21 the solitary metastatic lesion located subpleurally in the left lower lobe was removed by wedge resection. The patient made an uneventful recovery. Microscopic examination of the specimen removed showed teratoma involving the lower lobe of the left lung. At the time of thoracotomy there was no evidence of any mediastinal or hilar lymph node involvement. The patient is alive and apparently free from cancer at the present time, three months after the pulmonary resection.

SUMMARY

The patients presented had a large variety of primary lesions. We now realize that one of them could have had the metastasis treated as effectively by irradiation (Case 2). Two patients did not undergo resection of the primary extrapulmonary neoplasm (Cases 1 and 2) and were treated with irradiation and radium application only. In both instances no recurrence of the neoplasm locally was observed at the time the pulmonary metastases made their appearance. The time interval between the irradiation treatment and the recognition of the pulmonary metastases was 10 and two years, respectively.

Three patients had involvement of one of the major bronchi giving symptoms mimicking primary bronchogenic carcinoma arising in a major bronchus. At the time of exploration three patients had spread of the metastatic neoplasm to hilar lymph nodes. This particular observation emphasizes the fact that such lesions should be resected when first seen and that any delay in time is as detrimental as

it would be if one were dealing with a primary bronchogenic neoplasm. So far as regional node metastases are concerned, the metastatic pulmonary lesions behave very much like primary pulmonary malignant growths.

In three patients symptoms of severe hypertrophic pulmonary osteoarthropathy developed (Cases 1, 2, and 7). This was the main reason for exploration in one case (Case 7), leading to resection of bilateral lesions, with remarkable improvement.

There was one immediate postoperative death (Case 1). One patient died one year and 10 mo. after resection of the pulmonary lesion which had metastasized from an epidermoid carcinoma of the nasopharynx and four years after initial therapy for the nasopharyngeal tumor. This patient had two pregnancies during the period of observation (Case 2). Two additional patients are alive now with evidence of intrathoracic recurrence of the neoplasm but without evidence of local recurrence (Cases 4 and 8). Five patients are at present alive and well.

SUMMARY AND CONCLUSIONS

In order to prevent pain and lengthen life, there are times when it is of value to remove pulmonary lesions which have metastasized from malignant neoplasms primary elsewhere in the body. The indications for such an operative procedure are complex, but they will become clearer as more experience is gained with particular lesions and with the passage of time. Nine cases are presented, with short-term follow-up studies revealing that some patients have benefited considerably from such procedure and that others have obtained questionable relief.

COARCTATION OF THE AORTA

A Study of Seventy Cases in Which Surgical Exploration was Performed

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SIX YEARS have now elapsed since Crafoord [1] in Sweden and Gross [2] in this country independently did the first successful operations to remove the strictured segment in coarctation of the aorta. The ingenuity and pioneering of these two men deserve much credit, for prior to their work coarctation of the aorta was looked on only as an interesting entity for which little could be done in the way of treatment. Since the hypertension produced by the coarctation is due to a mechanical obstruction, it falls into that small group of hypertensive conditions for which surgery may offer a cure. Therefore, by removal of the obstruction and reestablishment of the vascular channel many patients may be given the opportunity of a longer and healthier life.

In the past four and a half years surgical intervention for the correction of coarctation of the aorta has been undertaken by one of us (Clagett) in 70 patients. It was thought that a study of this group might shed some light on the problems confronting the surgeon when dealing with this condition.

AGE

The youngest patient who underwent operation was 7 yr. of age, and the oldest was 50. The average age, however, was 24½ yr. One patient was less than 10 yr. of age, 20 patients were aged 10 through 19, 35 were 20 through 29, and 13 were 30 through 38. Exploration was done on one patient 50 yr. of age, but correction of the coarctation could not be performed. The optimal time for surgical intervention, we believe, is between 15 and 20 yr. of age. Among patients younger than this we fear that the anastomotic site may not grow as fast as the rest of the aorta, thereby producing further stricture. In patients more than 20 yr. of age sclerotic

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1. Crafoord, C., and Nylin, G.: Congenital Coarctation of the Aorta and Its Surgical Treatment, J. Thoracic Surg. **14**:347-361 (Oct.) 1945.

2. (*a*) Gross, R. E.: Surgical Correction for Coarctation of the Aorta, Surgery **18**:673-678 (Dec.) 1945. (*b*) Gross, R. E., and Hufnagel, C. A.: Coarctation of the Aorta: Experimental Studies Regarding Its Surgical Correction, New England J. Med. **233**:287-293 (Sept. 6) 1945.

changes have already begun to occur which greatly increase the hazards of the operation. However, our tendency now is to extend the age limit further and further and not to deny an older person the benefit of surgical intervention if his general condition warrants it. Several persons who have successfully undergone surgical treatment at the Mayo Clinic had previously been turned down at other places because of age.

SEX

Just as patent ductus arteriosus occurs predominantly in females, coarctation of the aorta is seen most commonly in males. The usual ratio cited is three or four males to every female. In our series there were 44 males (63%) and 26 females (37%), a ratio of less than 2:1.

FAMILY HISTORY AND PATIENT'S PAST HISTORY

Several points in the family histories were of interest. Two patients had brothers who died suddenly after extreme exertion. One of them was only 35 yr. old, and the other was known to have had hypertension. Unfortunately, no necropsies were performed. One patient's twin brother died at birth, presumably of some congenital abnormality, while the sister of another patient died of congenital heart disease.

The past histories of the great majority of patients were conspicuously noncontributory. Most had been in good general health all their lives, and more than half had undergone such operations as appendectomy, tonsillectomy, mastoidectomy, herniorrhaphy, and submucous resection without incident. A diagnosis of rheumatic fever was made during childhood in five cases, but in all likelihood many of the symptoms and physical findings were those of the coarctation, since none of the patients in these five cases presented rheumatic valvular disease at the time of operation. Prior to operation for their coarctation nine patients had 13 pregnancies and four Caesarean sections. Only two patients had toxemia. Benham [3] has recently reviewed 53 cases recorded in the literature of pregnancy occurring in patients with coarctation and has added three cases of his own. In his opinion therapeutic abortion is unjustified and Caesarean section at term before labor begins is the treatment of choice.

SYMPTOMS

Unlike patients with some other types of congenital heart disease, persons born with coarctation of the aorta appear for the most part to be normal and healthy. Indeed, some excellent athletes have had this defect without ever being aware of its presence. Therefore, it was not surprising to find that 19 of our patients were asymptomatic and that 23 were practically asymptomatic when they came to operation. Among those presenting symptoms (Table 1) easy fatigability and dyspnea on exertion headed the list. Headache, aching or tiredness in the calves, and palpitation were the next commonest symptoms, followed in close order by cold feet, precordial distress, dizziness, tachycardia, and blurred vision. A few patients presented multiple symptoms, while others had to be questioned in detail before admitting to some of the foregoing symptoms.

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3. Benham, G. H. H.: Pregnancy and Coarctation of the Aorta, J .Obst. & Gynaec. Brit. Emp. **56**:606-618 (Aug.) 1949.

TABLE 1.—*Symptoms Registered by Patients Who Had Coarctation of the Aorta*

Symptoms	Patients
Easy fatigability	23
Dyspnea on exertion	23
Headache	18
Tiredness, aching, tingling, weakness in calves	18
Palpitation	17
Cold feet	13
Precordial pain or tightness	9
Dizziness	8
Tachycardia	6
Blurred vision	6
Nervousness	6
Dyspnea at rest	4
Pressure, pain or heaviness in abdomen	3
Epistaxis, full feeling in head, numb hand.....Each,	2
Tinnitus, pulsation in ear and finger tips, flushed face and neck, swollen feet, hands, face.....Each,	1

PHYSICAL EXAMINATION

In recent years the tendency has been to rely more and more on laboratory determinations and roentgenologic interpretations in arriving at a diagnosis. As a result, the art of physical diagnosis has been relegated to a back seat. However, in the case of coarctation of the aorta all that is needed to enable one to make the diagnosis is a stethoscope, a sphygmomanometer and one's fingers.

The great majority of patients were well developed and well nourished. Only three were obese, while four were frail. Elevated systolic and diastolic blood pressures were found in the arms, while the systolic pressure in the thighs was low. The diastolic pressure in the thighs, however, was usually higher than normal.

The commonest cardiac murmur heard was over the base of the heart and was systolic in character. Thirty-seven patients had such a murmur, while in seven others the systolic murmur was loudest at the apex. In 23 cases the systolic murmur was of such intensity as to be equally prominent at the base and at the apex. The murmur was transmitted into the vessels of the neck in 30 cases. In only 3 cases of the 70 was there no cardiac murmur. Accompanying the systolic murmur in 15 patients was a diastolic murmur, being at the base in 14 and at the apex in one. Twelve of the basal diastolic murmurs were presumably due to insufficiency of bicuspid aortic valves, while two were due to a patent ductus arteriosus. Of note also was the fact that one patient with patent ductus arteriosus presented no diastolic murmur.

The intercostal arteries as a rule were so dilated as to be conspicuous on physical examination. In 19 patients the pulsations of these arteries could be seen with the naked eye as well as heard through a stethoscope and palpated. In 12 patients these arteries could be palpated and heard but not seen, while in 22 their presence could be detected only by listening for the bruit over the vessel, usually in the interscapular region next to the spinal column. In 17 cases no bruit could be heard. Pulsation in the abdominal aorta was absent in almost all the 70 patients, and that in the femoral, popliteal, posterior tibial, and dorsalis pedis arteries was markedly diminished.

The electrocardiogram was nonspecific, although 27 patients showed left axis deviation and in 12 others a disturbance of the normal cardiac rhythm was revealed. Right axis deviation was present in one patient who had an associated patent ductus arteriosus.

ROENTGENOLOGIC EXAMINATION

The roentgenogram of the thorax can give much valuable information as to whether one is dealing with a coarctation of the aorta and in many cases is diagnostic. The changes seen are the result of the increased collateral circulation and the added strain forced on the heart. These changes often take years to manifest themselves to the fullest, and hence thoracic roentgenograms of children with coarctation often appear normal. In our series, however, only one thoracic roentgenogram was negative, and this was on a woman 33 yr. of age, who presented little evidence of collateral circulation. Notching of the inferoposterior margin of the ribs occurred in 65 of the 70 patients, a hypoplastic aortic knob in 28, and an enlarged left ventricle in 27. Recently Stauffer and Rigler [4] have called attention to the dilatation of the left subclavian artery in the posteroanterior thoracic roentgenogram and also its pulsation seen on roentgenoscopy and roentgenkymography. In their opinion this sign is pathognomonic of coarctation and is of particular value in the absence of rib notching. We have noted it in many of our roentgenograms.

Roentgenoscopy was done in 12 cases, in three of which it aided in making a diagnosis of patent ductus arteriosus in addition to coarctation of the aorta by revealing prominent hilar pulsations and some degree of right ventricular enlargement. Cardiac catheterizations were undertaken in four cases in which the diagnosis of congenital cardiac anomalies other than coarctation was entertained. In one case patent ductus arteriosus was confirmed.

The lungs in all cases were normal roentgenographically, with the exception of two patients who had calcified lesions which proved at the time of operation to be old granulomas. Excretory urograms done in some of the early cases were all normal.

Angiocardiography has been recommended [5] as being of value in establishing the diagnosis of coarctation of the aorta. We subjected four patients to angiocardiography; the stricture was well outlined in three of them. However, the procedure is not a simple one and is not without its risks. We feel that the ultimate treatment will not be influenced and that a diagnosis can be made in all cases of coarctation without resorting to such an added test. Unfortunately, an inoperable lesion can be determined only under direct vision at the time of operation, when the size, position and aneurysmal dilatations of the intercostal arteries can be accurately appraised. One patient came to us for operation, bringing with him angiocardiograms taken elsewhere which showed the coarctation extremely well. From the angiocardiograms it appeared that a subclavian-aortic anastomosis would have to be done. However, an end-to-end aortic anastomosis was accomplished without undue difficulty, illustrating further the limitations of angiocardiography.

4. Stauffer, H. M., and Rigler, L. G.: Dilation and Pulsation of the Left Subclavian Artery in the Roentgen-Ray Diagnosis of Coarctation of the Aorta: Roentgenkymographic Studies in 13 Cases, Circulation **1**:294-298 (Feb.) 1950.

5. Epstein, B. S.: Angiocardiography: Its Application to the Diagnosis of Coarctation of the Aorta, Radiology **54**:211-218 (Feb.) 1950.

ASSOCIATED CONGENITAL ANOMALIES

Two congenital anomalies are classically associated with coarctation. They are bicuspid aortic valves and cerebral aneurysms. There were 13 such valves and eight cerebral aneurysms in our series of cases. Of the 13 bicuspid aortic valves one was proved at necropsy and 12 were suspected on the character of the basal diastolic murmur. Likewise, one cerebral aneurysm was verified at necropsy, and seven were believed on clinical grounds to be present. Five of the patients had cerebral vascular accidents, and two were afflicted with epilepsy.

Three of the patients, two of whom were male, had an associated patent ductus arteriosus. Two of the vessels entered the aorta distal to the coarctation, and one entered proximal to it. All three vessels were divided between Pott's clamps, and the ends were sutured with two rows of silk. There were at least eight other cases in which a small vessel in the ligamentum arteriosum remained patent and required a ligature.

The only other congenital anomalies recorded were in three patients presenting an undescended testis, a double vagina and cervix, and an ectopic left kidney which was found to be lying on top of the bladder.

DIAGNOSIS

The diagnosis of coarctation of the aorta is easy to make. It does not require elaborate laboratory procedures, as do many of the other cardiac abnormalities. The essential thing is to think of coarctation as a possible diagnosis, particularly when one is confronted with hypertension and cardiac murmur in a young person.

Half of our patients had known that they had hypertension for a year or more (one for 25 yr.) before the diagnosis of coarctation was entertained. The correct diagnosis was made by local physicians in 22 cases, by consultants elsewhere in 20 cases, and by us in 28 cases. Seven patients were referred specifically for sympathectomy, five were referred because of essential hypertension, four because of hypertension occurring during pregnancy, two with the diagnosis of rheumatic valvular disease, and one came because a roentgenogram made by a mobile unit revealed an enlarged heart. Of interest also was the manner in which the hypertension had been first detected. The armed forces had rejected 20 patients because of high blood pressure. These patients had previously considered themselves well. The first mention of hypertension in 13 other patients had been made during routine school examinations. Insurance, preemployment, civil service, 4-H Club, and Red Cross blood bank examinations had revealed the hypertension in 11 more cases.

PREOPERATIVE COMPLICATIONS

As most persons with coarctation are relatively asymptomatic, it follows that preoperative complications are for the most part minimal. Of those confronting us (Table 2), the myocardial defects were most prevalent. Three patients exhibited right bundle-branch block and another a sinoauricular block. Two patients were epileptic, two had residua of recent cerebrovascular accidents, and one had had a recent subarachnoid hemorrhage. Three had been in congestive failure, or were on the verge of going into it, while two had hypochromic anemia. It is important to

TABLE 2.—*Preoperative Complications Exhibited by Patients Who Had Coarctation of the Aorta*

Preoperative Complication	Patients
Right bundle-branch block	3
Epilepsy	2
Hypochromic anemia	2
Residua of recent cerebrovascular accident	2
Recent subarachnoid hemorrhage	1
Cerebrovascular accident without residua	1
Recent congestive failure	1
Borderline cardiac failure with patent ductus arteriosus	1
Sinoauricular block	1
Impaired conduction of myocardium	1
Recent auricular fibrillation and decompensation	1
Recent paroxysmal tachycardia and pneumonitis	1
Obesity	1
Extreme nervousness	1
Mild hypomania	1
Anxiety with chronic invalid pattern	1

stress that none of these complications prompted us to deny operation to these persons. These were the ones who needed surgical treatment the most, and the operative mortality rate was far from prohibitive.

TREATMENT

The responsibility for advising surgical treatment of these patients places a heavy burden on the surgeon. As we have commented, the majority of patients found to have coarctation of the aorta have been well most of their lives and feel perfectly healthy at the time of examination. We do not know the long-term results of operation for coarctation of the aorta, and patients are inclined to wonder at the necessity for surgical intervention. On the other hand, there is no other treatment for the condition whatsoever, and a study of what happens to patients without surgical treatment more than justifies the calculated risks.

Maude Abbott's classic work on congenital heart disease included 200 patients with coarctation of the aorta, of whom 148 had died before the age of 40 yr. More recently Reifenstein, Levine and Gross [6] reviewed 104 cases of coarctation in which necropsy had been performed, with the following interesting results: Twenty-six per cent of the patients lived to an average age of 47 yr. with little or no incapacitation; subacute bacterial endocarditis developed in 22%, and they died at an average age of 28 yr. (in 40% of the cases of coarctation there were bicuspid aortic valves), and 23% died a sudden death from rupture of the aorta at an average age of 27 yr. The fourth group of 29% comprised the patients in hypertensive states. One-third of these died of a stroke at an average age of 28 yr., while two-thirds succumbed to heart failure at an average age of 39 yr. When these figures are taken into consideration, surgical intervention appears to be entirely justifiable and should be strongly urged.

6. Reifenstein, G. H.; Levine, S. A. and Gross, R. E.: Coarctation of the Aorta: A Review of 104 Autopsied Cases of the "Adult Type," 2 Years of Age or Older, Am. Heart J. **33**:146-168 (Feb.) 1947.

ANESTHESIA

In all cases nitrous oxide, oxygen and ether were the agents employed. More recently, induction has been performed with pentothal sodium. Intratracheal tubes are used in all patients. Two 15 gage needles are placed in veins ready for immediate transfusion in case of sudden, severe hemorrhage.

TECHNIQUE

A long, curved posterolateral incision on the left was made in all cases, and the scapula was retracted upward. In 48 cases (most of the recent ones) a long segment of the fifth rib alone was resected. The posterior portion of the fourth rib was resected in 14 cases when additional exposure was needed. In the remaining eight cases various portions of the fifth and sixth ribs were removed to obtain adequate exposure. The collateral circulation encountered in the muscles was often astounding, and considerable time had to be devoted to accomplishing hemostasis. The pleural cavity was usually entered through the bed of the fifth rib, and the aorta in the region of the coarctation was dissected free of the mediastinal pleura, special care being taken not to injure the intercostal arteries, the thoracic duct or the left vagus and left recurrent laryngeal nerves. The ligamentum arteriosum, which draws the strictured segment anteriorly and medially, was routinely divided.

The coarctation in every case occurred between a point just distal to the origin of the left subclavian artery and a point 2.5 cm. beyond it, the average distance being 1.5 cm. From 1 to 2 cm. of aorta (average length, 1.5 cm.) was resected, the diameter of the aorta at the strictured site varying from 0.3 cm. to complete stenosis. The aorta was usually arteriosclerotic, and often a large yellow intimal plaque was present at the site of coarctation. When the aorta was being freed sufficiently to apply the Pott clamps and later to approximate the cut ends, from no to three intercostal arteries below the stricture had to be sacrificed. The sacrificed intercostal arteries were from both sides, though more on the left were severed than on the right. An occasional bronchial or esophageal artery also needed dividing. The intercostal arteries in a person who has coarctation are among the most sclerotic, friable and dangerous arteries that one encounters in all surgery, and great respect must be paid to them at all times.

The anastomoses were accomplished with an intima-to-intima continuous everting mattress stitch using 00000 silk. Preliminary to this, three to four interrupted everting mattress sutures were placed to act as a guide. On completion of the anastomosis removal of the lower clamp was done first, followed shortly by removal of the upper one. The latter was released slowly but usually was off in less than one minute. We have not encountered cardiac embarrassment after this relatively rapid removal of the proximal clamp, as has been experienced by Gross.[2a] In some patients a drop in blood pressure of 40 to 80 mm. of mercury occurred immediately on release of the clamps. Absorbable gelatin sponge (gelfoam®) was placed in the region of the anastomosis in 45 cases to assure hemostasis. Oxidized cellulose (oxycel®) and thrombin were used once. The mediastinal pleura was loosely sutured over the site of anastomosis, and 240,000 units of penicillin were placed in the thoracic cavity. An average of 500 cc. to 1,000 cc. of blood was administered to the patient during operation, although some patients did not require any blood, while others needed as much as 2,500 cc.

Blalock and Park[7] in 1944 were the first to propose anastomosing the left subclavian artery to the aorta after resection of the coarctation. One of us (Clagett[8]) did the first such operation in a human patient in 1946. However, the vascular bed was not increased to any great extent, since the blood was shunted from the many well-developed collaterals associated with the left subclavian artery. Consequently, this operation has been largely abandoned, and in the last 48 operable cases an end-to-end anastomosis has been performed. In eight of the 62 operable cases in this report the left subclavian artery was incorporated into the anastomosis, while in 54 the ends of the aorta were sutured together.

POSTOPERATIVE CARE

The postoperative care of these patients has been relatively simple. Fluids given intravenously have been limited to 1,500 cc. on the day of operation. The following day fluids and food are given by mouth. A 30 F. mushroom tip intercostal catheter placed at the time of operation so as to drain the pleural space is usually removed in 48 hr. Three hundred thousand units of procaine penicillin are given daily for about a week. Patients usually dangle their legs over the side of the bed on the fourth postoperative day, are up and about on the fifth day, and leave the hospital on the 10th to the 12th day.

POSTOPERATIVE COMPLICATIONS

The commonest complication following operation was transitory hoarseness. This was encountered in eight cases. Minor trauma to the left recurrent laryngeal nerve, with edema, was probably responsible for it. In no case was the change in the voice permanent.

An interesting complication occurred in a woman aged 25 yr., who on her fifth postoperative day had a subarachnoid hemorrhage. After a month of strict rest in bed and sedation she improved greatly and left for home asymptomatic with a blood pressure of 120 mm. of mercury systolic and 70 diastolic. One might speculate on the possibility that the hemorrhage was due to a rupture of a congenital cerebral aneurysm, which might have occurred had she undergone no operation at all. If this were the case, the diminished hypertension as a result of her operation may have protected her from a subsequent fatal hemorrhage.

A strange thing also happened in the case of a woman aged 33 yr., who presented relatively little evidence of collateral circulation preoperatively and whose operation was one of the most satisfactory from a technical standpoint. On the ninth, 10th and 12th postoperative days, however, sudden, intense, burning epigastric pain developed. The pain would last for about an hour and then subside, leaving her extremely weak. Physical examination, the electrocardiogram and routine laboratory studies and thoracic roentgenograms were all negative. The source of the abdominal pain was never accounted for, but apparently the condition was not serious and not related to the reconstruction of the aorta.

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7. Blalock, A., and Park, E. A.: The Surgical Treatment of Experimental Coarctation (Atresia) of the Aorta, Ann. Surg. **119**:445-456 (March) 1944.

8. Clagett, O. T.: Coarctation of the Aorta: Surgical Aspects, Proc. Staff Meet., Mayo Clin. **22**:131-135 (April 2) 1947; The Surgical Treatment of Coarctation of the Aorta, Proc. Staff Meet., Mayo Clin. **23**:359-360 (July 21) 1948.

Obstructive pneumonitis involving the whole right lung occurred on the second and again on the 23rd postoperative day in one patient. In another, massive collapse of the left lung occurred immediately after operation but responded well to the insertion of an S needle into the pleural space for suction. Chylothorax developed in one patient, but it subsided spontaneously after several thoracenteses of more than 2,000 cc. of fluid. One superficial wound infection and one acute thrombosed hemorrhoid complete the list of postoperative complications.

RESULTS OF OPERATION

It is not the aim of this paper to evaluate the results obtained after surgical excision of the coarctation. Recently Hallenbeck and his co-workers [9] have done this for the first 31 patients in the series of cases being presented here. Essential to such a critical analysis, in their opinion, are the preoperative and postoperative blood pressure studies and pulse wave contours recorded in the radial and femoral arteries by means of intra-arterial needles, with the use of the strain gage manometer.[10] In this manner also one may dispense with the ordinary cuff method of determining blood pressure, which is notoriously unreliable. Such objective criteria as these for measuring improvement after operation are far better than subjective changes in the patient's clinical course. This is particularly true in coarctation of the aorta, since the symptoms are few to begin with and the organic changes, such as cardiac enlargement and rib notching, do not regress postoperatively. Also, what often appears to be a good clinical result is not confirmed as such by the laboratory studies.

Gross,[11] in reporting on the results obtained in his first 106 patients surviving operation, stated that 97 were completely cured, eight obtained fairly satisfactory relief, and one patient got no relief whatsoever. Hallenbeck and his co-workers, commenting on our first 31 patients, found that 50% were cured (blood pressures 130 mm. of mercury systolic and 90 diastolic or lower) while 94% were clinically cured or improved (blood pressures lowered significantly and consistently but not as low as 130 mm. of mercury systolic and 90 diastolic). One extremely important point to be kept in mind is that it sometimes takes months for the pressures to return to normal. A further point of interest brought out by both groups is the better results attained with the end-to-end aortic anastomosis than with the use of the left subclavian artery. Often when the latter is used a simultaneous onset of radial and femoral pulse waves is accomplished but no drop in the blood pressure is noted.

INOPERABILITY

Of the 70 patients on whom surgical exploration for coarctation of the aorta was performed, eight were found to have inoperable lesions at the time of exploration, an inoperability rate of 11.4%. This rate compares favorably with the experience of Gross,[11a] whose inoperability rate for 130 patients was 9.2%, particu-

9. Hallenbeck, G. A.; Wood, E. H.; Burchell, H. B., and Clagett, O. T.: Coarctation of the Aorta: The Relationship of Clinical Results to Cardiovascular Dynamics Studied Before, During, and After Surgical Treatment, Surg. Gynec. & Obst. **92**:75-80 (Jan.) 1951.

10. Brown, G. E.; Clagett, O. T.; Burchell, H. B., and Wood, E. H.: Preoperative and Postoperative Studies of the Intraradial and Intrafemoral Pressures in Patients with Coarctation of the Aorta, Proc. Staff Meet., Mayo Clin. **23**:352-358 (July 21) 1948.

11. (*a*) Gross, R. E.: Surgical Treatment in 130 Cases of Coarctation of the Aorta, Tr. A. Life Insur. M. Dir. America **33**:83-98, 1949; (*b*) Coarctation of the Aorta: Surgical Treatment of 100 Cases, Circulation **1**:41-55 (Jan.) 1950.

larly since he used human arterial grafts,[12] in 12 cases, with 10 good results. Too long and tapered a strictured segment, hypoplasia of the aorta distal to the coarctation, aneurysmal dilatations of the intercostal arteries at their junction with the aorta, and huge intercostal arteries present at the site where we should have liked to place our clamps were all reasons why we were unable to correct the coarctation of the aorta in these eight cases. In some of the cases we might have been able to complete an anastomosis had we had a graft ready for immediate use. However, in other cases we feel that even the availability of a graft would not have helped us out of the dilemma.

One case deserves special mention. It is that of a woman aged 50 yr. who appeared physically to be 15 yr. younger than her stated age. She had had a cerebrovascular accident a year prior to operation. At operation a 1 cm. aneurysmal dilatation of the first left intercostal artery was present at the point where the artery sprang from the aorta. This area was scarred and adherent, probably as a result of previous hemorrhage. While the mediastinal pleura was being gently dissected away, a dissecting aneurysm of the aorta developed, beginning at the site of intercostal aneurysmal dilatation and spreading downward beneath the diaphragm before our very eyes. Needless to say, we did not delay in terminating the operation. Surprisingly, the patient made a slow but uneventful recovery. However, no high hopes are being held for her future.

MORTALITY RATE

There have been five surgical deaths among the 70 patients on whom exploration for coarctation was performed, a mortality rate of 7.1%. All the deaths occurred among the first 15 patients who underwent operation. The last 55 operations undertaken have not resulted in any deaths. Gross has had 12 deaths among the 130 patients on whom he has performed exploration, a mortality rate of 9.2%. However, in his last 50 cases only two patients have died. Cardiac failure and hemorrhage account for most of his deaths, as is true in our series.

One of our patients died on the operating table from heart failure, while two others succumbed to heart failure on the first and 14th postoperative days, respectively. Separation of the anastomosis, occurring on the ninth and 34th postoperative days, respectively, was responsible for the remaining two deaths. One of the two patients died on the operating table during an attempt to repair the anastomosis.

COMMENT

While no definite attempt has been made to canvass these 70 patients for a follow-up study, we have heard from the great majority of them by mail a number of times since operation. Several interesting features are worthy of mention. Two patients became pregnant nine and 19 mo., respectively, after operation. The first had a normal term pregnancy and an uneventful labor and puerperium. Elective outlet forceps were used. Her blood pressure at no time rose above 130 mm. of mercury systolic and 78 diastolic. The other patient likewise had an uncomplicated

12. Gross, R. E.; Hurwitt, E. S.; Bill, A. H., Jr., and Pierce, E. C., II.: Preliminary Observations on the Use of Human Arterial Grafts in Treatment of Certain Cardiovascular Defects, New England J. Med. **239**:578-579 (Oct. 14) 1948. Swan, H.; Robertson, H. T., and Johnson, M. E.: Arterial Homografts: I. The Fate of Preserved Aortic Grafts in the Dog, Surg. Gynec. & Obst. **90**:568-579 (May) 1950.

pregnancy, during which she gained only 20 lb. (about 9.1 kg.), had no edema or albuminuria, and had a blood pressure which varied from 140/80 to 180/96. An elective Caesarean section at 38 wk. was done with the patient under caudal anesthesia before the onset of labor. This is the procedure that we recommend. Another patient of ours was six months pregnant when this paper was written. One young woman entered nurse's training seven months after her operation and has so far been able to carry a full program without undue strain. Three other female patients have undergone further surgical procedures. One underwent uterine suspension and removal of fibroids two years after her operation at the clinic, while another was forced to have an emergency laparotomy for a twisted ovarian cyst only three weeks postoperatively. The third woman required surgical intervention for a protruding intervertebral disk in the lumbar segment of the spinal column. All three withstood the added surgical procedures without incident, and their convalescences were smooth. One of our patients has applied for group life insurance, and when last heard from was being favorably considered.

SUMMARY AND CONCLUSIONS

The diagnosis of coarctation of the aorta is easily made and requires no special laboratory procedures. It is necessary, however, that one think of the diagnosis when examining a young person who has hypertension. It is our opinion also that angiocardiography adds little in helping to establish the diagnosis and need not be used. Patients with coarctation of the aorta should not be denied the benefits of surgical treatment because of advanced age, myocardial conduction defects, previous cerebrovascular accidents or previous congestive failure. Resection of the strictured segment of aorta with end-to-end anastomosis is the treatment of choice. In our study of 70 cases of coarctation of the aorta in which surgical exploration was performed 11.4% were found to be inoperable at the time of exploration, while the mortality rate was 7.1%. However, in the last 55 cases exploration has been performed without any deaths.

DISCUSSION

Dr. Egbert H. Fell, Chicago: Dr. Clagett asked me to open the discussion of this interesting paper presented by Dr. Jampolis. One is indeed envious of the large number of cases of coarctation which they have studied and treated so well. Of great interest is the age groups which they have cared for, and with the average age 24½ yr., they have concluded that the optimum time for surgery is between 15 and 20 yr. of age. One patient was under 10 yr. Of the six patients on whom we have operated, five were under 15 yr. of age and one was 24.

I believe that the patients with symptoms of any severity should be operated on regardless of age, even in the early months of life, and in our limited experience those under the age of puberty do better than the older age groups and have less associated acquired pathologic changes due to the strictured aorta with its resulting hypertension, arteriosclerosis, vascular accidents and cardiac injury.

To illustrate how early cardiac damage may take place, the following slides will show photographs of the postmortem studies of a 3 mo. old child that was seen with Dr. Benjamin M. Gasul at the Mount Sinai Hospital (the postmortem study and the excellent kodachrome® slides are credited to Dr. Davidson and his associates of the department of pathology in that hospital). Clinically the child had an adult coarctation of the aorta, an enlarged heart and recent bronchopneumonia. Death occurred within 24 hr. of admission. The history was that of cardiac failure. In such cases a dissection of the stricture and end-to-end anastomosis using interrupted sutures should give a good result. We are observing another infant with coarctation and an enlarged heart, but he is progressing satisfactorily; in case there is evidence of clinical change this infant should receive the benefit of an operation.

The second case that illustrates the importance of early operation concerns a boy 9 yr. of age whose systolic blood pressure in the upper extremities was 200 to 210 mm. of mercury; no pulse or blood pressures were obtained by the cuff method in the lower extremities. At operation an enlarged sclerotic aorta overlay the stenosed aorta. While the ligamentum arteriosum was being freed from the aorta, this sclerotic area tore, requiring two ligatures of the aorta at this point. Arteriosclerosis occurs early in life in congenital cases.

A 15-yr.-old girl, considered to be healthy, awoke one morning two and a half years ago with hemiplegia. A number of physicians were consulted as to its cause, and a neurosurgeon was unable to find the femoral pulse; the diagnosis was thus easily made. With the other patients operated on, she has made an excellent recovery.

Dr. James Hubly, of Battle Creek, Mich., a guest at this meeting, told me of the recent death of one of the athletes in their local high school. The congenital condition had not been recognized prior to autopsy. Death occurred at a swimming meet.

There is enough evidence in the literature to show that the aorta will enlarge during growth, and since irreducible pathological changes can be prevented by earlier operation we should encourage all physicians, particularly pediatricians and general practitioners, to add to their routine physical examinations palpation for the femoral pulse so that early diagnosis and treatment may give patients a better chance for normal life.

One of the following three slides will give direct evidence that in four of our six cases there was an enlarged left subclavian artery and would meet Stauffer and Rigler's criterion of a pathognomonic sign which Drs. Clagett and Jampolis reemphasize occurred in their series of cases. The next two slides are drawings showing stenosis of the left subclavian artery as it arises from the aorta, and the third slide shows the coarctation between the left common carotid, which is markedly dilated and thickened, and the subclavian artery, which is small. In the second and third cases there was no enlargement of the shadow of the left subclavian artery as seen on roentgenology or fluoroscopy. There was a lower systolic blood pressure in the left arm when compared with the right, and there was no notching of the ribs on that side. Both patients have made excellent recoveries.

Drs. Clagett and Jampolis found three patients in whom a patent ductus arteriosus was associated with a coarctation, with the ductus arteriosus patent distal to the stenosis in two. What were their ages? How do you classify the pathologic process? What were the clinical preoperative findings?

Twenty-seven patients reported on today showed left ventricular enlargement. What percentage of the patients had left ventricular strain on electrocardiographic studies? I believe left ventricular strain was present in all our cases, and I am sure that the 9-yr.-old boy previously mentioned showed marked strain on electrocardiographic study. We have a 13-yr.-old boy in the Presbyterian Hospital at the present time who has severe left ventricular strain.

It is my belief that the optimum time for surgery for coarctation of the aorta is prior to puberty, before strenuous activity is engaged in and while the vessels are elastic and have not encountered the severe arteriosclerosis that progresses so rapidly in adolescents and young adults.

COMMISSUROTOMY IN MITRAL STENOSIS

CONRAD R. LAM, M.D.
DETROIT

SINCE March 31, 1950, at this hospital 19 patients have been accepted for surgical treatment of the mitral valve. The word "commissurotomy" in the title indicates that of the several operative procedures described or recommended during the past few years, that of Bailey and his associates [1] has appeared to be the most practical. This method involves an auricular approach to the stenosed valve with inspection by "digital vision" and an attempt to widen the orifice by cutting at the angles or commissures without the sacrifice of any valve leaflet structure, thus avoiding the production or augmentation of regurgitation. A similar plan was also evolved by Harken [2] and by Brock,[3] although the latter has been inclined to do most of the splitting with the finger alone.

Two types of operation have been avoided. The first is the method of insertion of a valvulotome through the ventricular wall with resection of a portion of a valve leaflet. Cutler and Beck [4] used this procedure in four patients 25 yr. ago, and all died within a week. Smithy and his associates [5] have recently reported their experience with a punch type of valvulotome inserted through the ventricle or auricle. A review of their seven case histories indicates that the valve orifice was not enlarged in four cases, and in a fifth the only effect was to make worse the preexisting regurgitation. At the 1950 meeting of the Central Surgical Association, Murray [6] reported that he had operated on 10 patients with a cardiovalvulotome inserted through the left ventricular wall with the purpose of removing a portion of the posterior cusp. To compensate for the regurgitation thus produced, he sometimes inserted a new valve beneath the mitral, consisting of the palmaris longus

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From the Division of General Surgery of the Henry Ford Hospital.

Read at the Eighth Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

1. Bailey, C. P.; Glover, R. P., and O'Neill, T. J. E.: The Surgery of Mitral Stenosis, J. Thoracic Surg. **19**:16, 1950.

2. Harken, D. E.; Ellis, L. B., and Norman, L. R.: The Surgical Treatment of Mitral Stenosis: II. Progress in Developing a Controlled Valvuloplastic Technique, J. Thoracic Surg. **19**:1, 1950.

3. Baker, C.; Brock, R. C., and Campbell, M.: Valvulotomy for Mitral Stenosis, Brit. M. J. **1**:1238, 1950.

4. Cutler, E. C., and Beck, C. S.: The Present Status of the Surgical Procedures in Chronic Valvular Disease of the Heart: Final Report of All Surgical Cases, Arch. Surg. **18**:403 (Jan.) 1929.

5. Smithy, H. G.; Boone, J. A., and Stallworth, J. M.: Surgical Treatment of Constrictive Valvular Disease of the Heart, Surg. & Obst. **90**:175, 1950.

6. Murray, G.: Treatment of Mitral Valve Stenosis by Resection and Replacement of the Valve Under Direct Vision, Arch. Surg. **61**:903 (Nov.) 1950.

tendon covered with a vein with the intimal surface turned out. He stated that "the results in eight have been fairly satisfactory," two patients having died in the immediate postoperative period. This method of first producing insufficiency and then correcting it seemed unnecessarily complicated for our hands when the simpler procedure of commissurotomy was available.

The second type of operation that has not been used is that in which an attempt is made to create an artificial Lutembacher syndrome, i. e., to add an interatrial defect or its equivalent to provide a safety valve for the left auricle during periods of especially high pressure so that pulmonary edema may be prevented. Bailey and his associates [1] produced an interauricular defect large enough to admit the tip of the finger in one patient in whom commissurotomy appeared to be impractical, and the patient died in 60 hr. because of inability to keep up a systolic blood pressure which would sustain life. Harken [7] created atrial septal defects in two patients without immediate fatality, but no details or late follow-up observations were given. More attractive was the pulmonary vein-azygos anastomosis of Sweet and Bland.[8] Only one of six patients died, and the other five had immediate relief of pulmonary edema. The theoretical objections to such an operation, which relieves only one symptom of mitral stenosis, namely pulmonary congestion, have been well outlined by others,[1] who pointed out that patients with Lutembacher's syndrome actually live a hazardous life and the average age at death is only 40 yr., little longer than uncomplicated mitral stenosis expectancy. A follow-up report of the first cases of Sweet and Bland is awaited with interest.

OPERATIVE TECHNIC

In 19 cases, the mitral valve has been attacked by the method of Bailey and his associates,[1] with some modifications which will be described in detail. The anesthetic routine was suggested by Dr. Joseph Dondanville and was administered in most cases by Mrs. Lenore Gribble. Because of the presence of several pieces of electrical equipment used to study the physiological aspects of the operation, no explosive gas is used. Preoperative medication consists of ⅛ grain (8 mg.) of morphine sulfate and 1/150 grain (0.4 mg.) of atropine. The patient is rendered unconscious with an intravenous injection of thiopental (pentothal®) sodium with curare, after which the larynx is sprayed with 10% cocaine solution to permit intubation of the trachea. Further anesthesia is maintained with the thiopental solution and a 50-50 mixture of nitrous oxide and oxygen, which is changed to higher concentrations of oxygen if indicated. Continuous observations of the blood oxygen by the photoelectric oxyhemograph shows that unless the heart action is grossly inadequate satisfactory arterial oxygen saturation is maintained by the above method. Intravenous injection of procaine was used in only one case and then only after ventricular fibrillation appeared (Case 9).

The patient is placed on his back with the left hand under the body and the elbow in a right angle. On one occasion, the arm was placed above the head and temporary nerve damage was produced. The incision is below the breast and

7. Harken, D. E.; Ellis, L. B.; Ware, P. F., and Norman, L. R.: The Surgical Treatment of Mitral Stenosis: I. Valvuloplasty, New England J. Med. **239**:801, 1948.

8. Sweet, R. H., and Bland, E. F.: The Surgical Relief of Congestion in the Pulmonary Circulation in Cases of Severe Mitral Stenosis, Ann. Surg. **130**:384, 1949.

extends from the sternum to the anterior axillary line. After division of the pectoral muscles, the third rib is excised subperiosteally from the sternum to the midaxilla. The pleura is opened, and the second and fourth cartilages are divided. The pericardium is incised posterior to the phrenic nerve and a few cubic centimeters of 2% procaine hydrochloride solution is injected into the pericardial sac. Two minutes later, the pericardium is further incised to expose the pulmonary artery and the auricular appendage, both of which will be found to be dilated and under increased pressure.

Procaine is injected subepicardially around the base of the appendage, and two purse-string sutures of heavy braided silk on atraumatic needles are placed well

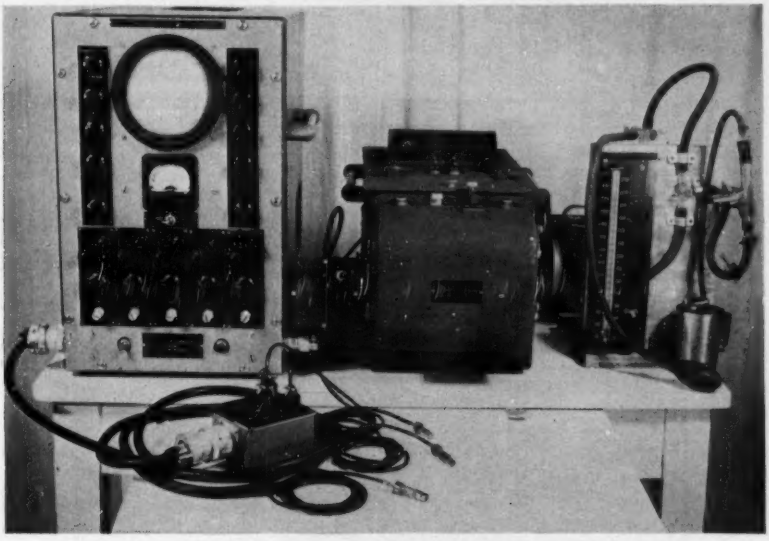

Fig. 1.—Impedance gauging system (Hathaway Instrument Company, Denver) which was used to observe and record physiologic pressures. On the left is the cathode ray tube and controls; in the middle, the recording camera (oscillograph); on the right, the calibration equipment, and in the foreground, the gauges to which the needles are attached.

down on the appendage. Precommissurotomy pressure determinations are then made with needles introduced into the pulmonary artery and the left auricle. For observing and recording these pressures, we have used the Hathaway impedance-gauging system [9] (Fig. 1). The wave form and pressure in each vascular chamber are observed directly on the face of the cathode-ray tube and recorded simultaneously with or without the electrocardiogram on photographic paper for later consideration. A record typical of severe mitral stenosis with a successful commissurotomy is shown in Figure 2. A tracing showing a considerable amount of

9. Schafer, P. W., and Shirer, H. W.: An Impedance Gauging System for Measurement of Biologic Pressure Variables, Surgery **26**:446, 1949.

unsuspected precommissurotomy regurgitation may be seen in Figure 3. The clinical features of this case (Case 4) are given below. A detailed study of the oscillograph records of the first 12 cases has been presented elsewhere by Dr. Edward R. Munnell (Research Fellow of the Michigan Heart Association) and me.[10]

After the pressure studies, a noncrushing clamp is placed on the auricle and the tip is amputated to permit the introduction of the right forefinger and the Bailey-Glover-O'Neill commissurotomy knife, which for reasons of hemostasis is passed through an opening in the palmar surface of a second rubber glove and out through

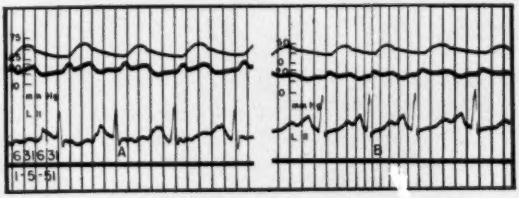

Fig. 2.—Oscillograph tracings in a case of pure mitral stenosis before and after a successful commissurotomy. Upper tracing, pulmonary artery; middle tracing, left auricle; lower tracing, electrocardiogram, lead II.

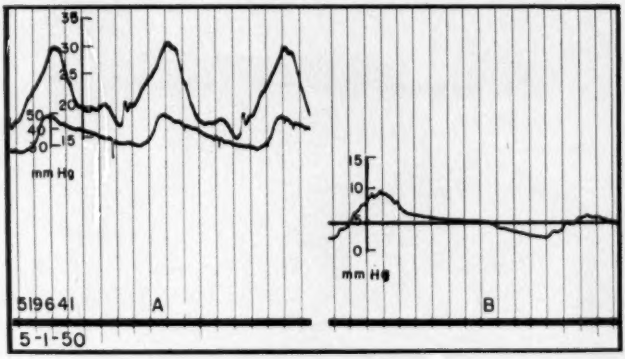

Fig. 3.—Oscillograph tracings of a case showing a large amount of unsuspected mitral regurgitation. *A*, before incision into the valve; upper tracing, left auricle; lower tracing, pulmonary artery. Note the sharp increase in auricular pressure synchronous with the pulmonary pulse. *B*, auricular pressure after attempted commissurotomy. (Case 4, patient died.)

the opened end of the glove finger. Four types of knives are available, three of which have the guillotine feature to facilitate the cutting of thick or calcified valves. The guillotine can be closed by a lever, by thumb pressure or by the turning of a rachet. My experience has been confined to the use of the rachet type. As originally constructed, the rachet was insecurely attached to the knife, and it came

10. Munnell, E. R., and Lam, C. R.: Cardiodynamic Effects of Mitral Commissurotomy, read at the Twenty-Third Annual Meeting of the Central Society of Clinical Research, Circulation, to be published.

off during the cutting of a commissure in one of the early cases (Fig. 4). The piece has been firmly attached to this particular instrument in our shop, and the manufacturer informs me that similar changes have been made on knives subsequently produced.

The modifications in technic referred to above have to do with the prevention of blood loss from the opening in the auricle. I found that this was more of a problem than would be supposed from published descriptions of the operation. The trouble was not with tearing or perforation of the auricular wall, which others have reported; in fact, I have found the appendage rather tough and convenient to suture. The leaking was chiefly between the two gloves, through the spaces unoccluded at the edges of the relatively thick commissurotomy knife. This hemorrhage could be largely prevented by having the first assistant place the first throw of a knot in the purse-string suture and pull tightly. However, this restricted free movement and accurate pressure sensations of the operator's hand. The assistant's hands could have been kept out of the incision by completing the square knot, but this would have made the purse-string suture useless for closure of the defect after the removal of the finger. We tried using a slip knot, but this invariably became

Fig. 4.—Commissurotomy guillotine, with broken ratchet. See text.

loose after manipulation and turning of the finger. The problem was finally solved by passing the ends of the purse-string sutures through a length of rubber catheter to make use of the snare principle (Fig. 5). After the finger and knife are well in the auricle, the assistant tightens one or both of the purse-strings and ties the ends over a piece of applicator stick. Further tightening would be possible by placing a clamp between the stick and the catheter. After the commissurotomy, the assistant cuts off the stick, quickly removes the catheter and ties the purse-string in the usual manner. I have found it comforting to have a second purse-string in place. In several cases, the first one has broken; in one instance, the post-commissurotomy tracings indicated a grossly unsatisfactory result and, since the spare purse-string was in place, the finger and instrument were easily inserted for the second time.

In spite of the advantages of the snare technic with the purse-string, there was still marked leakage of blood, which escaped out of the hole in the outer glove from which the knife emerged. At the suggestion of Dr. Edward R. Munnell, this source of bleeding was controlled by adding a sixth finger to the outer glove in the region between the thenar eminence and the forefinger, forming a tunnel through which the knife could be inserted and to the end of which a tight ligature could be applied (Fig. 6). Advancement of the knife through the glove resulted

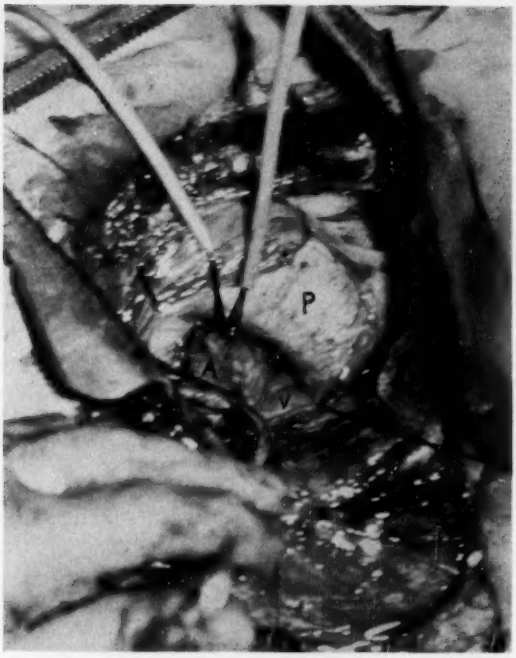

Fig. 5.—Photograph at operation, showing the purse-string sutures passed through pieces of catheter tubing for control of the auricular appendage. *A*, auricular appendage with non-crushing clamp applied to the tip; *V*, dilated pulmonary vein; *P*, pulmonary artery.

Fig. 6.—Six-fingered glove for use with the commissurotomy guillotine, designed and made by Dr. Edward R. Munnell.

in effortless telescoping of the added finger. In use, the outer glove becomes distended with blood but none escapes.

With the finger in the auricle and the purse-string tightened, the mitral orifice is explored. Regurgitation if present is easily detected. The general characteristics of the valve, including calcification, are noted. The degree of eccentricity of the valve opening gives the indication for medial or lateral commissurotomy or both. Before the knife is used, cautious attempts may be made to fracture the commissures with the finger. In three of my cases, the valve was felt to open nicely along the original lines of fusion. However, in one case (Case 17) the tear extended into the base of the cusp, producing a small amount of regurgitation. This would not have occurred if the pressure on the finger had been purely in the direction of the commissure instead of toward the ventricle. If further opening is indicated, the closed guillotine is inserted in the valve with the hand in marked supination. The degree of supination necessary to cut the anterolateral commissure can be reduced by tilting the table toward the operator. The guillotine is then opened and the blade caused to catch on the edge of the valve exactly at the commissure if possible. The valve is then cut with a sawing motion or by closure of the guillotine, usually the latter. Further cuts may be taken as indicated by palpation. After the completion of the lateral commissurotomy, the table is straightened, the hand is pronated again, and a decision is made as to the advisability of medial commissurotomy. With calcified valves, this will usually be necessary, while with fibrous, more supple valves lateral commissurotomy will usually suffice. In 19 cases, the following procedures were carried out: lateral incisions in 9 with medial finger fracture added in 2 cases; medial incisions in 3 with lateral finger fracture in 1; incisions in both commissures in 4 cases, and finger fracture only in 3 cases.

After the commissurotomy is done, the finger and knife are removed and the distal purse-string is tightened and tied. It seldom produces complete hemostasis, but the small orifice remaining is easily closed with the finger-tip until a running suture is placed over the defect. The postcommissurotomy pressures in the pulmonary artery and auricle are then observed and recorded. Both should show a reduction in pressure, and the wave form of the auricle should indicate that no regurgitation has been produced. The ends of the spare purse-string are then cut off, blood is removed by suction from the pericardial and pleural cavities, penicillin is added, and the chest is closed in the usual manner. In most of the cases closure without drainage has been used, but in almost all early thoracentesis for hemothorax has been required; the use of underwater catheter drainage for a few days has much to commend it.

SELECTION OF CASES AND RESULTS

The ages of the patients accepted for commissurotomy fell into the following groups: 20 to 29 yr., 1 case; 30 to 39 yr., 12 cases; 40 to 49 yr., 5 cases; over 50 yr., 1 patient (aged 53). Only 10 patients gave a history of rheumatic fever. All had many of the disabling symptoms of mitral heart disease, including shortness of breath, orthopnea, and marked decrease in the ability to do work. Seventeen had had definite attacks of pulmonary edema, and all except one of these had had hemoptysis. Eight had auricular fibrillation at the time of operation. All had the typical diastolic rumble at the apex, and nine had a systolic murmur at the apex

of grade 2 or better. Fluoroscopic examination in most instances showed a picture typical of mitral stenosis, with enlargement of the pulmonary conus, left auricle and right ventricle. Three of the deaths occurred among the five patients with evidence of hypertrophy of the left ventricle. In many of the patients the pulmonary artery pressure was determined by cardiac catheterization; the mean pressures varied from 54 to 124 cm. of water. Space does not permit a discussion of the other physiological studies which were carried out and their possible significance.

Of the 19 patients operated on, 17 were found to have stenosis as the predominant lesion of the mitral valve, but two of these had significant regurgitation. Two other patients had gross regurgitation and little stenosis. Both of these patients and one of those with significant incompetence did not survive. Of the 15 patients with pure mitral stenosis, 12 are considered to have good or excellent results, one was temporarily improved and two died in the immediate postoperative period. One of the patients whose heart function was restored to normal as far as physical signs are concerned has residual focal brain damage due to embolism or thrombosis, which, unfortunately, affected the speech center especially. There are five deaths and two unsatisfactory results in living patients to be explained, if possible, in the following history abstracts.

CASE 3.—B. L., a woman aged 40 yr., was known to have heart involvement since an attack of rheumatic fever 14 yr. before. She had become completely disabled, with symptoms of shortness of breath, paroxysmal attacks of pulmonary edema with hemoptysis, marked orthopnea and ankle edema. The examination on April 4, 1950, was described as follows: "There is a tinge of cyanosis. There is a grade 2 mid-diastolic rumble at the apex and a harsh grade 4 systolic murmur also maximal at the apex transmitted into the axilla and generally over the precordium. The liver is tender. The impression is that rheumatic heart disease with mitral stenosis and insufficiency with auricular fibrillation is present." Although it was recognized that this patient was not a good candidate, she was accepted for commissurotomy. At operation, the first oscillograph tracings indicated regurgitation, and this was confirmed by the exploring finger. The orifice was stenotic and calcified. Difficulty was encountered in placing the knife in the irregular opening, and recourse was had to finger dilatation. The valve was felt to open until it accommodated the forefinger. Because the heart action was poor, the finger and knife were withdrawn. The heart began to beat vigorously, but progress oscillograph tracings showed that the dilatation had increased the amount of regurgitation to an alarming degree. It was felt that the rigid ovoid orifice had been converted into a round one. Since it was obvious that the patient could not live with this situation, the auricle was entered again and this time a cut was made in the lateral commissure. This apparently broke the rigid ring so that the leaflets could approximate better, and the final pressure tracings showed a low auricular pressure. This patient was improved after operation, and she could lie flat in bed for the first time in years. There was no cough, and she walked without dyspnea. The systolic murmur at the apex was less intense, but a diastolic rumble persisted. About two months after the operation, she was hospitalized for heart failure, and 10 mo. later was still confined to a chair. In retrospect, since this patient was accepted for operation in spite of the suspected regurgitation, the results could not have been worse and probably would have been better if a more radical commissurotomy to include the medial end had been done. A stiff, calcified valve should have both commissures cut.

CASE 4.—H. F., a man aged 46, was found to have rheumatic heart disease in 1947, after he had been short of breath for three years. There was no history of rheumatic fever. The early observers described a grade 3 apical systolic murmur and a grade 4 diastolic rumble. In 1950, most of the examiners mentioned only the diastolic murmur. The usual symptoms of mitral stenosis became so severe that he became incapacitated and was accepted for operation, which was done on May 1, 1950. The precommissurotomy and postcommissurotomy tracings are those in Figure 3. Exploration with the finger confirmed the marked regurgitation and

revealed a very irregular calcified valve, into which the guillotine was inserted with difficulty. Three times the blade was impinged against the lateral commissure and closed, but it was felt that nothing was accomplished. The knife was turned around and two cuts were made in the direction of the medial commissure, after which it was felt that the mitral ring had been opened considerably. The regurgitation was less to the palpating finger and in the final oscillograph tracing. This patient died with dyspnea and cyanosis 37 hr. after the operation. The autopsy showed a grossly deformed valve (Fig. 7), with a mass of calcium and scar tissue at the lateral commissure and a fairly satisfactory cut at the medial end. There was also a contusion of the ventricular wall opposite an osteophyte of a vertebral body.

Case 5.—M. B., a woman aged 46, was known to have heart disease for 16 yr. In 1947 fibrillation was present and she was described as having a grade 3 apical systolic murmur and a rumbling diastolic murmur. On April 4, 1950, the following account was given of her condition: "There is moderate cyanosis. The neck veins are full, and the abdomen protrudes with ascites. The liver pulsates 16.5 cm. below the costal margin. There is auricular fibrillation.

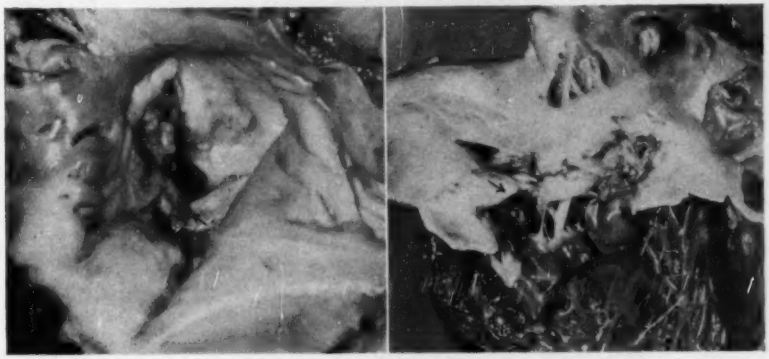

Fig. 7.—Autopsy specimen showing the mitral valve in Case 4. On the left the arrow points to the incision into the medial commissure; the calcified irregularity of the lateral commissure is well shown. The picture on the right shows the valve opened with the posterior leaflet in the middle. The arrow indicates the surgical incision, which extended up onto the auricular endocardium.

There is a rough systolic murmur at the apex and a loud diastolic rumble. The symptoms suggest far advanced congestive failure associated with mitral stenosis and insufficiency. The immediate outlook is poor." The patient was refused as a candidate for commissurotomy at first but was finally accepted. Commissurotomy was attempted on May 17, 1950. The blood pressure was 80/60 before the induction of anesthesia and was unobtainable as the operation proceeded. The patient was found to have tight mitral stenosis of the fibrous type, and the lateral commissure was cut. Unfortunately, the mechanical failure of the guillotine described above occurred while an attempt was being made to cut the medial commissure. Since the heart action was poor, it was deemed advisable to discontinue further efforts to cut the valve. After closure of the chest, the patient was cyanotic but the blood pressure had risen to 86/50. She recovered consciousness but died in 17 hr. Autopsy showed that both commissures had been cut for a distance of 6 mm., but considerable stenosis remained.

Case 8.—A. P., a woman aged 45, had been known to have rheumatic heart disease for 10 yr. She had had attacks of hemoptysis since 1934. Examination on March 24, 1950, showed auricular fibrillation, the typical signs of mitral stenosis, pulmonary emphysema and fibrosis. Cardiac catheterization revealed that the pressure in the right main pulmonary artery was 109 cm. of water at rest and 123 cm. after exercise. Dr. Mason Sones, who carried out the physiological studies, stated: "This patient has severe organic pulmonary fibrosis and emphysema, and it is felt that her pulmonary hypertension is not merely the functional result of her mitral stenosis. Because of this, we would not expect any remarkable reduction in pulmonary

hypertension after operation. There would appear to be no contraindication to surgical intervention, although her prognosis as to functional improvement is not good." In spite of this warning, operation was carried out on June 26, 1950. Only a medial commissurotomy seemed to be feasible. Oscillograph tracings showed no change in the pulmonary artery pressure and no change in the wave form of the auricle, although the pressure was lower. This patient was temporarily improved but became disabled in a few months. It is thought that she has pulmonary insufficiency as well as residual mitral stenosis.

CASE 9.—M. D., a woman aged 53, had rheumatic fever at the age of 12 and had been known to have heart involvement for 40 yr. The typical signs of mitral stenosis were present in 1937. The blood pressure in that year was 155/90; in 1941, 164/90; in 1946, 175/90; in 1948, 225/95,

Fig. 8.—The mitral valve in Case 9, showing severe incompetence. The arrow indicates the small cut in the lateral commissure. Note the huge auricle.

and in 1950, 180/105. On May 11, 1950, her condition was described as follows: "She is unable to sleep. The legs are swollen above the knees. The heart is thumping. A grade 3 systolic murmur is heard in the aortic area, less well at the apex. The presystolic rumble is audible. Auricular fibrillation is present." With considerable misgivings, the patient was accepted for operation. During the placement of the purse-string, the ventricles began to fibrillate. Normal rhythm was finally restored with manual production of systole and intravenous injection of procaine solution, but before the auricle was opened there were two other periods of ventricular fibrillation, for a total of 40 min. In spite of this distressing complication, the finger and knife were inserted in the auricle, only to disclose the discouraging fact that there was little stenosis and a patulous valve permitting marked regurgitation. A small token cut was placed in the lateral commissure before the auricle was closed. The patient recovered consciousness but died in 12 hr. with pulmonary edema. Autopsy showed a valve hopelessly incompetent (Fig. 8).

CASE 14.—R. S., a man aged 30, had rheumatic fever at the ages of 6 and 16. At 17, he had purulent pericarditis, with a Streptococcus of the viridans group in the culture. Four years before, he had ascites, presumably on the basis of constrictive pericarditis. Eight months before, he began to have more ascites, finally requiring paracentesis every two weeks. Examination on June 5, 1950, revealed the presence of auricular fibrillation, a systolic murmur at the apex and a rough diastolic murmur at the apex. Fluoroscopy showed that the heart was grossly enlarged, with a giant left atrium which displaced the esophagus to the right of the midline and posteriorly. In spite of contradictory catheterization data, it was decided that the principal lesion was mitral stenosis and exploration was done on Nov. 17, 1950. Adhesive pericarditis was encountered, and partial decortication was carried out to expose the left side of the heart. After tedious dissection, it was possible to explore the valve in the usual manner, and it was disappointing to find that the main difficulty was regurgitation. A token cut was made in the lateral commissure, and it was hoped that the patient would live to have a more thorough decortication of the heart through a midline sternotomy incision. However, he died on the fourth postoperative day with cyanosis and air hunger. Autopsy showed a valve almost identical with that of the heart shown in Figure 8.

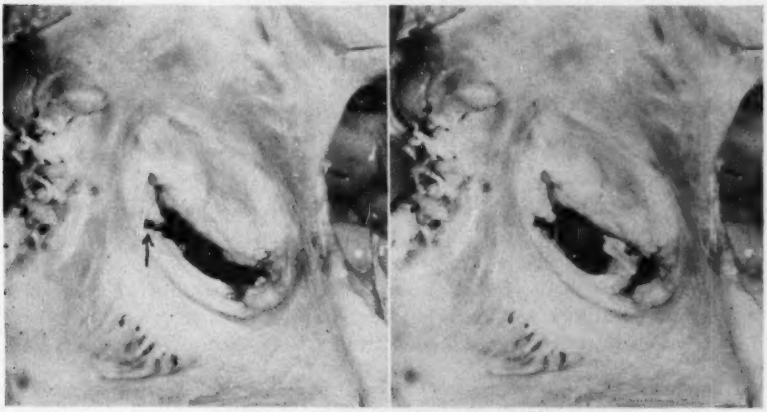

Fig. 9.—Two views of the mitral valve in Case 17. On the left, the arrow points to the cut which had been aimed at the lateral commissure but which actually cut through the edge of the posterior leaflet. Medially, there appears to be a satisfactory "finger fracture," but the picture on the right shows how the tear in the commissure entended around the base of the leaflet.

CASE 17.—M. C., a woman aged 34, had had scarlet fever at the age of 17 and had had progressive dyspnea since 1942. There was a chronic cough with occasional hemoptysis. Walking produced a sensation of choking. Examination of Dec. 27, 1950, revealed a regular cardiac rhythm, a grade 4 systolic murmur at the apex transmitted to the axilla, and a mid-diastolic rumble. Cardiac catheterization showed a mean pulmonary artery pressure of 106 cm. of water. Pulmonary ventilation studies revealed that the relation of resting minute volume to maximum minute volume was only 1:2, as compared with a normal of 1:8. The oxygen absorption at rest was 2.73%, and at maximum ventilation, only 2.53%. These findings were thought to indicate severe pulmonary insufficiency. Commissurotomy was carried out on Jan. 3, 1951. The mitral valve was tight, and no insufficiency was noted. When the valve was dilated, there was splitting of the medial commissure in what appeared to be a satisfactory manner, but it was disappointing to feel that some regurgitation had been produced at the medial end of the valve. This decreased as time went by. A small cut was made in what was thought to be the lateral commissure. The patient's postoperative course was marked by the presence of cyanosis and

air hunger. There were several attacks of severe chest or heart pain, relieved by morphine. The patient died suddenly on the sixth postoperative day. Autopsy showed that not only had the medial finger fracture torn the commissure but the opening had extended posteriorly across the base of the leaflet (Fig. 9). It was certain that this piece was not being dislocated upward while the finger was in the auricle or it could have been palpated; however, it may have become misplaced subsequently. Microscopic examination of the lungs has revealed advanced sclerosis of the pulmonary arteries. If it had not been for the accident at the medial commissure, the case could be considered a parallel one to that described by Welch, Johnson and Zinsser,[11] in which an apparently ideal commissurotomy was followed by the death of the patient, presumably from irreversible pulmonary changes.

COMMENT

The unsatisfactory results must be explained on the basis of poor selection of the candidates for commissurotomy or technical errors during the operations. A review of the seven case histories given above would lead one to classify the failures in Cases 4, 5, 9 and 14 as being due entirely to case selection. In Case 4 there was marked regurgitation; in Case 5, terminal heart failure; in Case 9 the patient was 53 years of age with hypertension and mitral regurgitation, and in Case 14 the patient had adhesive pericarditis with regurgitation. In retrospect, two patients (Cases 5 and 9) should not have been accepted for any type of surgical treatment, and the patient in Case 14 might better have had a decortication of the pericardium primarily, although there is no assurance that he would have survived this with his mitral disease. One patient (Case 4) had a hopelessly deformed valve which was incompetent, but there seemed to be no way of establishing this fact without exploration. Two patients (Cases 8 and 17) showed evidence preoperatively of marked organic pulmonary damage, but so have others who have received benefit from commissurotomy. Furthermore, it is admitted that a more radical operation might have been possible in Case 8 and the tear in the posterior leaflet may have been very significant in Case 17. In Case 3 there was regurgitation preoperatively, but a better result might have been obtained with a more extensive commissurotomy.

SUMMARY

Nineteen patients have been operated on in an attempt to relieve the symptoms of mitral stenosis. The reasons for selecting commissurotomy, the method of Bailey and his associates, have been outlined. Two suggestions for the control of bleeding from the auricle have been made. Five patients died, and a review of the circumstances indicates that case selection was an important factor in the unfortunate results. The cardiac function of all of the other patients was improved in the immediate postoperative period, but two have since had recurrence of symptoms. With further knowledge of how to choose cases, commissurotomy by the auricular approach should be accompanied with a low mortality rate and a high percentage of improvement in persons disabled with mitral stenosis.

DISCUSSION

DR. EGBERT H. FELL, M.D., Chicago: I hesitated to accept Dr. Lam's invitation to open the discussion of his paper concerning commissurotomy because to date we have not found a patient with mitral stenosis who meets the criteria for operation. Drs. Bailey, Glover and

11. Welch, K. J.; Johnson, J., and Zinsser, H.: The Significance of Pulmonary Vascular Lesions in the Selection of Patients for Mitral Valve Surgery, Ann. Surg. **132**:1027, 1950.

O'Neill, of Philadelphia, have contributed a great chapter to cardiac surgery by devising this procedure and successfully operating on a good number of patients with this extremely disabling disease.

We have been interested in this problem, and, having seen Dr. Bailey and his group at work, we were anxious to perfect our technique and find candidates for surgery. At the Presbyterian and Cook County Hospitals we have studied the clinical, autopsy and museum specimens. Pure mitral stenosis, I can assure you, is a rare lesion. We cannot expect to find it, but it must be predominantly so, without marked mitral regurgitations or aortic disease, and it must not be associated with active rheumatic disease or endocarditis. There must not be an enlargement of the left ventricle or indications of left ventricular hypertrophy or strain. Perhaps we have been overcautious in our choice of cases, but the teachings of those with experience, we believe, are sound.

In response to Dr. Lam's invitation, I stated that I would discuss the pathologic changes in a museum specimen showing the nearest to the ideal mitral lesion I could find which would be benefited by surgery.

(Slide) This fish mouth opening of the mitral valve is rigid and thickened for about 4 mm. about the orifice. The rigid opening allows for some regurgitation. The photograph, when one is looking from above down, reveals normal-appearing tissue peripheral to the diseased mitral orifice. The commissures are well shown; commissurotomy into this nonsclerotic area is the procedure that Dr. Bailey has shown to be of benefit. Also, the close proximity of the normal-appearing aortic valve is seen. Injury to this septum is fatal.

(Slide) The photograph of the stenosed valve from the ventricular side shows the chorda tendinea, which if injured may cause death, and the close proximity to the aorta; again, the normal-appearing tissue peripheral to the narrowed fish mouth opening is well displayed.

The procedure that Dr. Bailey has perfected and that Dr. Lam is reporting today is a surgical procedure that attacks the pathologic process directly with "tactile vision" and is most logical.

FLEXOR TENDON GRAFTING TO THE HAND

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DIVISION of the flexor tendons within the digital sheath of the hand is a rather common injury, and its repair is a real challenge to the surgeon interested in trauma of the hand. The tendons divided retract and separate widely, and to obtain these separated ends and to unite them within the strict confines of the dense fibrous sheath of the digit creates a difficult problem. To secure union of the separated tendons within the sheath and later to hope for a gliding mechanism to provide flexion is almost a paradox.

It is rarely possible to perform a primary end-to-end suture of the flexor tendon within the digital sheath. It is felt that these injuries should not be repaired after two hours from the time of trauma or if unwise first aid has been administered. Search for the separated ends requires the enlargement of incisions and the opening of new areas, while suturing a poorly vascularized tissue in the presence of potential infection or actual contamination may be contributing to factors which are not desirable. Therefore, when the surgeon is in doubt as to the time, type of wound and character of first aid, it is better to cleanse carefully, excise and accurately close the soft tissue wound and at a later date undertake the repair which is so necessary. In the few cases fulfilling the requirements for successful repair the suturing has been done by the method suggested by Mason.[1] This method is to decompress the fibrous sheath at the site of union after suture of the tendon has been done and satisfactory results have ensued.

Unsuccessful results in this area of "no man's land" in the hand are rather common after primary end-to-end repair. It is felt that failure is due to injudicious, early, active motion before three weeks or results because moderate separation of the tendon ends has created excessive callus formation at the site of union so that the tendons become adherent within the fibrous tendon sheath. Occasionally, the surgeon may attempt to suture the sublimis and profundus tendons within the fibrous sheath, and this creates a large callus whose bulk prohibits motion. Sometimes failure may also follow when a midline incision has been made over the digit and palm, for this leaves a long, volar area of adhesions plus the late sequelae of contracture of the scar.

Since there are definite limitations to primary suture of tendons within the fibrous sheaths of the digits, it becomes the major consideration of the surgeon

Read at the Eighth Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

1. Mason, M. L.: Primary and Secondary Tendon Suture, Surg., Gynec. & Obst. **70**:392-402 (Feb., Pt. 2A) 1940.

to obtain kindly and early healing of the soft parts so that repair may be later performed. This healing requires careful attention to the usual surgical principles of cleanliness, excision and accurate closure of the soft parts; after sound healing has occurred, a secondary repair may be undertaken within three to four weeks after injury. However, before secondary repair may be done, the immediate inflammatory reaction must have subsided from about the wound. The small joints must be mobile, and there must be sufficient soft tissue remaining in order to allow accurate closure after excision of the scar. If infection has developed in the initial wound, repair should not be considered until the inflammatory reaction has completely subsided. In an avulsing type of wound in which the soft parts have become hard and indurated and the broad scar fixed to the deep structures, it is not feasible to anticipate movement of the repaired tendon within this type of tissue. Such a wound would require shifting of adjacent, sound, soft tissue or the application of a pedicle flap before tendon grafting could be undertaken. The outstanding factors which must be considered for late repair of these injuries is the sound healing of the wound, proper placing of incisions, the identification and freeing of the retracted tendons, and the preservation of sufficient fibrous tendon sheath to act as pulleys within the digit.

There is a great difference between repair within four to six weeks from the time of the injury and repair from within four to six months, or later. The earlier time limit is the most ideal for here the tendon ends, though separated, are not fixed solidly to the surrounding structures and may be easily released. The muscles of the retracted tendons have not become permanently shortened, and there is almost normal resiliency of these muscles at this time. Further, the fibrous tendon sheath within the digit has not collapsed, and this important structure may be readily identified and the normal tunnels recreated with ease. However, a different set of conditions exist when there has been delayed healing of the soft parts and it becomes necessary to perform operation many months after the injury. At this late date, the fibrous sheath has become collapsed and the recreation of a tunnel is technically a formidable problem. The muscles at the later date are fixed, and there is a myostatic contracture which handicaps the motor power of the graft. Finally, at this later time, the tendons are frozen in their position and are solidly adherent to the surrounding structures, more particularly at the divided ends. This fact again draws attention to the importance of observing the many small details in performing a primary repair of the soft part wound, for unless normal, primary healing occurs a necessary delay results and the surgeon is confronted with a tedious technical surgical procedure as contrasted with the far simpler operation performed within three to four weeks.

After three to four weeks, the retracted tendons are seldom in condition to permit the performance of an end-to-end suture within the digit. This is so because the tendons, when once retracted and allowed to remain in a relaxed position, become thickened and irregular in contour, with fine but definite adhesions to the surrounding structures. Swelling of the tendon precludes its use within the confines of the fibrous tendon sheath. Further, the roughening created by the adhesions which have been liberated would again cause fixation within the sheath. Therefore, it is felt that delayed or secondary repair of these injuries demands the insertion

of a tendon graft as such a procedure brings normal tendon into the digit and does not require a line of union of tendon ends to be placed within the limits of the fibrous tendon sheath.

One of the principal technical considerations to be commented on is the placement of the incisions on the digit and on the hand. This is emphasized because the incisions must be placed at both levels to allow identification and mobilization of the separated tendons and to admit adequate exposure of the sites of union of the tendon graft, both in the digit and in the palm. It is necessary to recall that incisions on the digits should follow well along on the radial or ulnar aspects. They may cross the digit at any site, but, again, they do so parallel to the lines of flexion creases. In order to expose the entire length of the tendon sheath within the digit, the incision may start across the distal pulp space, continue proximal to the radial

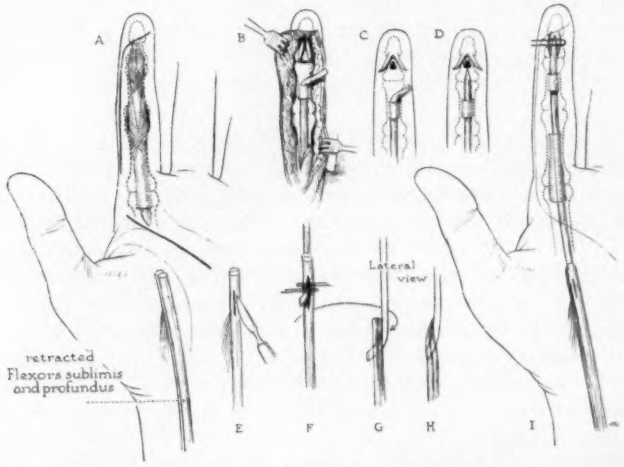

Fig. 1.—*A* shows suggested level of incisions on the digit and on the palm. *B* is the schematic representation of the tendon sheath and the tendon graft drawn into the digital bed. The distal segment of the profundus tendon has been made into an inverted "V." *C* is the site of removal of the periosteum from the volar aspect of the distal phalanx. *D* shows the sharpened tendon graft ready to be drawn into the apex of the retained original profundus tendon. This is now ready to be united by interrupted white silk sutures as shown in *I*. *E*, *F*, *G*, and *H* show the manner of attachment of the small tendon graft into the proximal motor tendons, united with fine white silk mattress sutures.

or ulnar aspect of the finger and then be extended down to the level of the web space. A second incision, the palmar portion, is made just proximal to the metacarpophalangeal joint and is so placed that it is parallel to the flexion creases of the palm. When the thumb is to be operated on, the incision is made similar to that on the digit and is carried down to the level of the web space, while the second incision is made at the level of the wrist and parallel to the flexion creases of the wrist. These incisions are placed so that contractures do not follow. It is granted that a midline incision is technically easier for the surgeon, but it becomes a severe catastrophe to the patient.

The incision on the digit is carefully performed, for the digital nerve and vessels must be identified and protected. Occasionally, the digital nerves have been divided and mobilization and later suture at the time of closure will be required. After the nerve has been identified, a thick flap is carefully raised and the fibrous tendon sheath is uncovered. This sheath tissue must be protected and preserved throughout the operation, for it is the vital structure which provides the necessary pulley action for a successful, functioning tendon graft. When this sheath is seen early, it may be partially collapsed and filled with old blood, but it is not a difficult problem to reproduce a tunnel. When the sheath must be opened to procure the ends of the retracted tendons, it should be done in such a manner as to remove a small block of this fibrous structure. It is imperative that the sheath tissue be preserved at the levels just proximal to each interphalangeal joint and at least a centimeter of this structure over the midportion of each of the proximal and middle phalanges. In patients operated on late, after several months, the sheath will be found collapsed, and to create a tunnel may require opening of the sheath. This is best done by dissecting it free at either the ulnar or the radial side where the structure attaches to the periosteum. In these late cases a flap of sheath may be raised at the necessary

Fig. 2.—*A*, laceration of the right index finger after 24 hr., with division of both flexor tendons and ulnar digital nerve. Excision was performed immediately and delayed closure of the soft-part wound only four days later. Three months later the inflammatory reaction had subsided, the joints were mobile, and at this time a tendon graft taken from the foot was inserted into the index finger. *B*, *C* and *D* show results of ability to flex and extend this digit. (By permission, American Academy of Orthopaedic Surgeons Instructional Course Lectures, Ann Arbor, Mich.: J. W. Edwards, Publisher, 1951, vol. 8.)

levels, and after the graft is placed in the new site then the flaps may be sutured over it and into normal position with fine interrupted silk sutures, reconstructing the pulley action of the sheath.

After the incisions have been placed on the digits and the palm, the retracted tendon ends are the next structures to be identified. The distal tendon end can be visualized within the sheath, and a block of this tissue not larger than half a centimeter is removed at the level of the proximal end of the distal segment of the flexor tendon and the adhesions between the tendon and the sheath are separated. This distal segment of the tendon is then freed and brought out at the level of the distal phalanx, the intervening sheath tissue being preserved. The proximal retracted tendon end is not as easily mobilized. In the early cases, however, in which operation is performed within four to six weeks, the tendons may be readily identified within the palmar wound and by gentle traction can be brought into the wound. In the later cases, several months after trauma, decided fixation of the distal end of the proximal segment will be noted. Freeing of this frozen tendon

may require a second window at the level of the web space or over the proximal phalanx of the digit so that the tendon end may be separated from the surrounding sheath tissue by sharp dissection. This separation usually requires dissection from both the palmar wound and the digital wound to free the tendon and obtain mobilization of this portion. The procedure can be troublesome at times, but careful, sharp dissection must be used throughout. When once the proximal segment of the retracted tendon has been freed, it is imperative that the palmar portion be mobilized so that there will be free gliding of this motor segment of the tendon. Free gliding is easily recognized in the earlier cases, while in the late repair the adhesions within the palm are more fixed and the myostatic contracture of the muscle within the forearm makes it most difficult to achieve anything resembling normal resiliency of the muscle. However, this segment must be freed of the adhesions and as much motion as possible of the proximal segment must be obtained. Occasionally, in the late cases, an enlarging incision in the palm may assist in freeing this segment.

The management of the sublimis tendon deserves some comment. When this tendon has been divided within the digit, leaving a segment of its distal portion

Fig. 3.—A healed laceration over the proximal phalanx of the left fifth digit with division of both flexor tendons within the digital sheath. *A* and *B* show ability to extend and flex. Tendon grafting was performed using a graft taken from the foot and inserted into this digit in the manner described in the text. *C*, *D*, and *E* show the ability to extend and flex this digit four months later.

inside the sheath, this distal portion then must be removed. When the sublimis tendon has been incompletely divided or roughened after the trauma, it also should be removed. However, there are a few cases in which the profundus tendon only has been injured by a laceration over the midphalanx and the sublimis tendon left intact. In these cases the sublimis tendon is allowed to remain and the tendon graft is threaded through the normal position occupied by the profundus tendon. The proximal portion of the sublimis tendon is handled as follows: Within the palm the sublimis tendon to the fifth digit is too small to be considered effective as a motor factor, while the sublimis tendon to the index, middle and ring fingers may be sutured side to side to the profundus tendon, thus reenforcing the motor power of the profundus tendon.

After mobilization of the tendon ends has been performed, a heavy suture is threaded through the fibrous tunnel of the digit from the distal phalanx to the level of the incision in the palm, and this suture is used later to guide the tendon graft into its new bed.

There are but few tendons which are satisfactory for use as tendon grafts. The proper length and size are the main requirements. The graft must be of sufficient

length to extend from the distal phalanx to the level of the palmar incision. A small but healthy tendon has great tensile strength and has proved competent for the later strength required of the digit. The small tendon graft has the added value of a modest disproportion between its size and the narrow limits of the fibrous tendon sheath, and so it is reasoned that there are less possibilities of adhesions to the sheath. At the present time, the long extensor tendons of the toes are the sources from which most grafts are derived. However, in a few cases, the palmaris longus may be used. The tendon graft is removed from the foot by exposing the entire extent of the desired length and not by placing two incisions and stripping the tendon from its bed. To strip the tendon by the latter method deprives it of the surrounding sheath and paratenon, which are indispensable to ultimate gliding of the tendons. A semilunar incision which completely uncovers the long extensor tendon is produced on the dorsum of the foot, and the desired tendon length is exposed and measured. A suture is placed through the long extensor tendon just proximal to the metatarsophalangeal joint, and the tendon is carefully dissected away from its bed, taking with it a generous amount of the sheath and the sur-

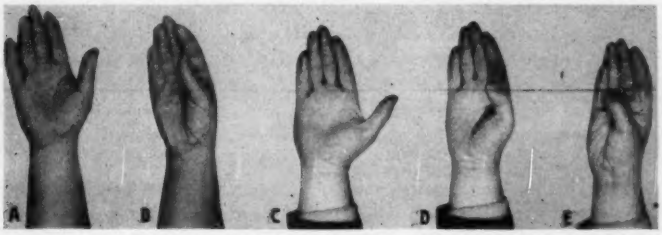

Fig. 4.—A healed laceration over the proximal phalanx of the right thumb three months after an unsuccessful attempt at primary repair of the flexor tendon of the thumb. There is division of the flexor pollicis longus and the digital nerves to the thumb. *A* and *B* show loss of flexion of the distal phalanx of the thumb, preoperatively. *C*, *D* and *E* show hand four months after tendon grafting and digital nerve repair.

rounding paratenon tissue. The required length of the graft is removed from the foot and is then inserted into the fibrous tunnel at the level of the palm, with the use of the previously inserted guide suture to lead it into position.

The method of attachment of the graft to the distal insertion of the flexor tendon is based on experimental work on the rate of healing of tendons [2] and also on the rate of healing of tendons to raw bone.[3] The tendon is attached in the following manner: The distal segment of the profundus tendon is isolated up to its insertion in the distal phalanx. This requires dissection of this segment almost to the level of the tuft of the phalanx. A deep, inverted "V" is made in this distal segment, and the apex of the "V" is at the distal extremity of the tendon. The "V" segment and the excess of the profundus tendon are removed, leaving two lateral slips of the distal segment, each measuring about 1 cm. In the apex of this area on the

2. Mason, M. L., and Allen, H. S.: Rate of Healing of Tendons: An Experimental Study of the Tensile Strength of Tendons, Ann. Surg. **113**:424-459 (March) 1941.

3. Hauser, C.: Rate of Healing of Tendon to Bone, Thesis, Northwestern University Medical School, 1949.

volar aspect of the distal phalanx the periosteum is carefully dissected away so as to leave a triangular-shaped area of raw bone. The tendon graft is drawn up to the level of the distal phalanx, and the end of the graft is sharpened so that it will insert into the previously prepared inverted "V," where it fits readily and so fulfills the requirement that raw tendon be attached to raw tendon and raw tendon to raw bone. The tip of the sharpened graft is placed in the apex of the inverted "V" of the profundus tendon and is sutured by four interrupted 00000 white silk sutures uniting the retained original lateral slips to the sides of the tendon graft. After the graft has been inserted into the distal segment, the digital wound is closed in layers and the digital nerves repaired, if necessary. After closure of the digital wound, the proximal end of the tendon graft is now ready to be inserted into the motor tendon. The graft is smaller than the proximal motor tendon and is inserted in the following manner because the disparity in size precludes the desirability of end-to-end suture. A small, stab incision is made through the proximal motor tendon, and the graft is threaded through this incision and attached at this level by two or three interrupted mattress sutures of white 00000 silk. The correct tension at which this graft must be sutured is always a problem. In a fairly early case, in which operation is performed within three to six weeks, there is freedom of the motor or proximal tendons and there is no fixation of the muscle. Naturally, in these cases a normal tension can be accurately judged. However, in the later case, in which there is not only fixation of the proximal tendon but also some muscle contracture due to disuse, the proper tension is much harder to judge. The following method has been used and is suggested: With only slight flexion of the wrist and moderate flexion of the involved digit, the tendon may be brought into satisfactory tension. Too much tension will necessitate acute flexion of all the structures and will result in slow separation of the tendon ends, while too much relaxation will not allow proper mechanical function. The palmar wound is closed in layers and the hand and wrist carefully maintained in the flexed position while a generous compression dressing is applied. This dressing will minimize hemorrhage, create gentle pressure and aid in diminishing postoperative edema. The hand and wrist are carefully splinted in a flexed position, care being taken that the digit operated on is firmly held to prevent extension. Experimental work has shown that the rate of healing of tendon grafts roughly parallels the healing in simple end-to-end suture of tendon. Absolute immobilization is maintained for a minimum of three and a half to four weeks before gradual relaxation is performed.

Postoperatively, physical therapy is used for from seven to 10 days, and the patient is then instructed in methods of home type of physical therapy such as washing the hand in warm, soapy water several times a day. Regardless of the physical therapy that may be used, in the final analysis it is the willingness and the desire on the part of the patient to obtain motion which is the most significant factor. When the patient once realizes that there is beginning motion, the steady increase in activity is readily apparent. It must be explained to the patient that movement begins slowly but that conscientious cooperation and effort on his part must be exerted for several weeks before full function is attained. During the first week or two little motion may be achieved, but with purposeful use of the hand the range of activity steadily increases.

SUMMARY

To accomplish free, gliding moving of tendon grafts within the digital area of the palm is a complicated problem. Restoring this movement requires attention to many small details. The manner of healing of the wound and the condition of the soft parts determine the time at which tendon grafting may be performed. Early grafting three to six weeks after trauma is a vastly different problem than that performed many months later. Proper placing of the incision, preservation of the tendon sheath, and minimal trauma in inserting the tendon graft are all of paramount importance and must be observed. Finally, the time of immobilization and the willing cooperation of the patient are extremely important if one is to obtain a good result from this challenging type of surgery.

TOTAL COLECTOMY FOR ULCERATIVE COLITIS

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THE TITLE of this paper may be somewhat misleading. No attempt is made here to suggest that total colectomy is the final word on treatment for ulcerative colitis, nor even to insinuate that it is the right treatment for the majority of patients suffering from this disease. However, when a ship is foundering, a life boat, though neither pleasant nor agreeable, may be the only hope. Similarly, when a life is threatened by severe intractable or fulminating ulcerative colitis, it has been found that it may be saved by the performance of a procedure which at first sight seems so radical as to make the bravest heart pause.

As in the case of most ailments, the ultimate treatment of ulcerative colitis will probably be determined only after the discovery of its primary cause. We may guess, but we cannot know, that this disease is a local manifestation of the failure of general bodily resistance, with a resulting attack on the colonic wall by organisms which are normally present within the colon but to which the healthy wall is immune. Perhaps we might suggest that this loss of resistance is due to a lessened blood supply to the colon following spasm of its vessels, which spasm is in turn caused by some central disturbance, either organic or functional, arising as the result of stress. It is certainly a striking fact that in every one of our intractable cases there has been a profound mental disturbance which has failed to yield to intensive psychiatric therapy. Strangely enough, after colectomy these patients seem to overcome their mental difficulties and have been able to resume work again. Perhaps the valley of shadow through which they pass acts as a shock treatment.

Whatever the cause of the disease, total colectomy is not recommended as a general cure for ulcerative colitis. We fully realize the mutilating nature of the procedure. It is advocated for those patients who, despite the most carefully planned medical and psychiatric measures meticulously and enthusiastically carried out, either continue to lose weight and strength or suffer from repeated colonic hemorrhages or perhaps for those who remain chronic invalids despite treatment.

Two fortuitous circumstances first suggested this procedure. In 1945 two patients were admitted to hospital suffering from fulminating ulcerative colitis. Medical treatment failed. An ileostomy was done, but both patients succumbed to the disease. However, after ileostomy but before death, the colon of each of these patients was washed out every day and the washings sent to the biochemist

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in the hope that some new light might be shed on the cause of colitis. He reported that these washings contained about 300 gm. of protein each day and later suggested that this protein loss contributed to the patient's death.

With this suggestion in mind and encouraged by one of us (G. G. M.) who had carried out several one-stage hemicolectomies with ileostomy for ulcerative colitis successfully some years before, we decided to carry hemicolectomy a step further and to remove as much of the colon as possible at one stage. This we did, the first patient to be operated on being a man of 22 with fulminating ulcerative colitis who had lost 2 liters of blood the day before operation. Despite this loss and though the bowel was perforated at the time of operation, the patient made an uneventful convalescence. This happy experience was followed in short succession by three others in which we had equally spectacular results.

Our medical colleagues were impressed with the results, and we established an arbitrary time of two months of medical and psychiatric treatment as being a fair trial. If improvement failed to occur in this time, the patient would be referred for operation. However, since then we have had two patients who lost nearly half their body weight within a month of the first symptom of the disease, one of whom became jaundiced before we finally operated. Therefore, we now set no arbitrary time as a waiting period but have suggested to the physicians that if the patient fails to respond promptly to medical and psychiatric treatment, a surgical opinion should be sought. We entirely concur with the idea that an early ileostomy alone may save some patients, but it has been our experience that neither physician nor patient is prepared to submit to this procedure until the disease is in a relatively advanced stage.

We do not wish to labor the technical features of an operation which you all know. The usual preoperative measures are carried out. The bowel is sterilized as well as possible by antibiotics, and large quantities of blood are on hand for the operation. A long midline or left paramedian incision is made excising the umbilicus. The colon is removed from the terminal ilium to the distal sigmoid in the simplest and easiest possible way. By first dividing the peritoneum on the lateral walls one may handle the bowel more gently and remove it more quickly, since one can then sever the arterial supply near its origin. Nevertheless, it has been our misfortune to perforate over half of the colons at the time of operation, so friable is the tissue. This has never prevented the patient's subsequent recovery, though it may make the postoperative course stormy. No attempt is made to reperitonealize the posterior abdominal wall. The ileostomy is formed through a stab wound somewhat to the right of where the umbilicus was. The sigmoid is delivered through a similar stab wound in the lower left quadrant. Patients are given the usual postoperative therapy.

Since we, along with Dr. Ripstein, commenced this series, we have carried out the procedure on 69 patients, with three deaths.

The group of 17 cases presented here have been followed for at least three years since operation. In all of them the acute fulminating type of disease or acute exacerbations of the chronic type were present. We have left out of this group all cases in which the operation was performed for chronic invalidism or for fear of the development of polyposis and possible cancer. In this series one death occurred. The patient involved taught us a lesion. We had carried out subtotal colectomy, but after considerable improvement the patient's condition remained static for six weeks,

when several perforations of the small bowel suddenly developed and he died of peritonitis. After autopsy the pathologist stated that the ulcers were not due to an ascending ileitis but were similar to those occurring in malnutrition. Just before the patient died, we washed out the terminal segment of the bowel and discovered that he was losing 100 gm. of protein a day.

We have had two similar cases since then but have been wise enough to perform an abdominal perineal removal of the terminal segment when the patients failed to gain. They immediately started to improve.

We have attempted an anastomosis in only one of this group of cases, and it was a failure. The disease immediately recurred. We have completed the operation by means of two-team abdominal perineal resection in five of our patients, and there are probably five others in which this should be done, although all of the patients are presently leading happy, useful lives. Nevertheless, the other five have symptoms either of failure to gain weight, pain in the back, discharge, bleeding, fistula, or polyposis, any one of which suggests that the operation should be completed. There have been no deaths from this secondary operation, but we worry about impotence.

It has been remarkable how well patients who have undergone an ileostomy have carried on with a Rutzen bag, which seems to cause them so little inconvenience. We have found the removal of the umbilicus of some value. Only one of the patients has had difficulty with the ileostomy; he suffered from continual bouts of intussusception until we performed another operation.

SUMMARY

We advocate more intensive medical and psychiatric treatment in the early phases of ulcerative colitis. The more advanced and rapidly progressive the disease becomes, the greater is the necessity for total colectomy, this dictum applying particularly to patients with acute fulminating disease. The operation of choice is a one-stage subtotal colectomy removing 6 in. (15 cm.) of the ileum and all of the colon to the lower sigmoid. This one-stage operation we believe to be preferable to preliminary ileostomy in that it immediately stops or greatly lessens both protein loss and toxic absorption.

It is probably seldom wise to restore the continuity of the bowel, and the patient should be so informed before the operation is performed. An ileostomy is a high price but relatively cheap when life itself is at stake.

Seventeen cases of acute fulminating ulcerative colitis are reported in which a one-stage subtotal colectomy was carried out, with a mortality rate of 5.8%.

In the entire series of 69 cases in which operation was performed by Dr. Ripstein and by us, there was a mortality rate of 4.4%. These operations were not all carried out for the acute type of colitis and consequently the mortality is lower.

VENOUS SHUNTS IN PORTAL HYPERTENSION

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THE USE of shunts between the portal venous system and the vena cava or its branches has become a well-established method of combating the complications of portal hypertension.[1] The impetus of a reasonable surgical treatment has resulted in an improved understanding of the modes of production of portal hypertension. The frequent disproportion between the level of the portal pressure in intrahepatic disease and the degree of hepatic damage has been studied by Kelty and others.[2] These workers find that the regeneration of liver cells which improves hepatocellular function adds to the interference with portal blood flow.

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1. (*a*) Whipple, A. O.: The Problem of Portal Hypertension in Relation to the Hepatosplenopathies, Ann. Surg. **122**:449-475, 1945. (*b*) Blakemore, A. H., and Lord, J. W., Jr.: Technic of Using Vitallium Tube in Establishing Portacaval Shunts for Portal Hypertension, ibid. **122**:476-489, 1945. (*c*) Blalock, A.: Use of Shunt or By-Pass Operations in Treatment of Certain Circulatory Disorders, Including Portal Hypertension and Pulmonic Stenosis, ibid. **125**:129-141, 1947. (*d*) Blakemore, A. H.: Indications for Portacaval Anastomosis—Analysis of Cases, Surg., Gynec. & Obst. **84**:645-653 (April) 1947. (*e*) Welch, C. S.: Technique for Portacaval Anastomosis (Eck Fistula), ibid. **85**:492-494 (Oct.) 1947. (*f*) Blakemore, A. H.: Portacaval Anastomosis, ibid. **87**:277-279 (Sept.) 1948; Portacaval Anastomosis—Observations on Technic and Postoperative Care, S. Clin. North America, **28**:279-289, 1948. (*g*) Learmonth, J. R., and MacPherson, A. I. S.: Surgery of Portal Hypertension: Account of 16 Cases, Lancet **2**:882-885, 1948. (*h*) Linton, R. R.; Hardy, I. B., Jr., and Volwiler, W.: Portacaval Shunts in Treatment of Portal Hypertension: Analysis of 15 Cases with Special Reference to Suture Type of End-to-Side Splenorenal Anastomosis with Splenectomy and Preservation of Kidney, Surg., Gynec. & Obst. **87**:129-144 (Aug.) 1948. (*i*) Linton, R. R.: Surgical Treatment of Bleeding Esophageal Varices by Portal Systemic Venous Shunts with Report of 34 Cases, Ann. Int. Med. **31**:794-804, 1949. (*j*) Blakemore, A. H.: Portacaval Anastomosis for Relief of Portal Hypertension, Surgery **26**:99-102, 1949; Portacaval Shunt for Relief of Portal Hypertension, Mississippi Doctor **27**:1-10, 1949; Preoperative Evaluation of Liver Function in Patients with Cirrhosis of Liver, Surg., Gynec. & Obst. **89**:357-359 (Sept.) 1949. (*k*) Julian, O. C., and Metcalf, W.: Nonobstructive Lateral Portal Vein-Vena Cava Anastomosis, Arch. Surg. **59**:433-436 (Sept.) 1949. (*l*) Pattison, A. C.: Use of Portacaval Anastomosis in Portal Cirrhosis, ibid. **58**:590-602 (May) 1949. (*m*) Welch, C. S.: Medical Progress: Portal Hypertension, New England J. Med. **243**:598-610, 1950.

2. Kelty, R. H.; Baggenstoss, A. H., and Butt, H. R.: Relation of Regenerated Hepatic Nodule to Vascular Bed in Cirrhosis, Proc. Staff Meet., Mayo Clin. **25**:17-26, 1950.

In cases of extrahepatic portal obstruction, the causes are narrowing down to those of congenital nature and those resulting from inflammation and thrombosis of the portal vein with subsequent organization along various lines. This organization may take the form of a single, extremely thick-walled vessel with small lumen, met with in one of our patients, or the formation of numerous thin-walled collateral venous channels, which we have encountered twice.

Many problems remain to be solved. The exact mechanism of portal hypertension is poorly understood in relation to the arterial inflow and venous obstruction components, to the possibility of direct arteriovenous communications in the diseased liver, and to the failure of the large new collateral venous mass to reduce the pressure. An understanding here is important to determine whether reduction of arterial inflow or decompression of the venous outflow from the splanchnic bed is the more physiologic treatment. The relationship between portal hypertension and ascites in liver disease is not clear, and as a result the weight of ascites as an indication for venous shunt has not been determined.

The important sequelae of portal hypertension are the esophageal and gastric varices, the secondary hyperplenism, and, questionably, the ascites. Of these, the bleeding which results from the varicosities constitutes the major danger to the patient. The mortality attendant on such bleeding is very high, and the apparent value of venous shunts in preventing further hemorrhages has been encouraging.

It is the purpose of this paper to present our experience with 27 cases of portal hypertension. The patients were subjected to operation, and in 21 instances a portal-systemic venous shunt was completed. Most of them had portal hypertension resulting from intrahepatic disease, Laennec's cirrhosis being the commonest cause. The majority of the patients were selected for operation on the basis of gastro-esophageal hemorrhage. Varices were demonstrated in 17 by means of a barium swallow or esophagoscopy. In cases in which there was no preoperative demonstration of varicose veins, the findings at operation confirmed the diagnosis of portal hypertension. The spleen was palpable in every instance in which the patient had not previously undergone splenectomy. Pancytopenia of secondary hypersplenism was present in 25% of the series. Thirteen of the 21 completed operations were performed on patients showing significant depression of liver function. Six of the completed operations and two of those not completed were performed on patients who showed preoperative ascites. In five patients the liver function was depressed severely, the test showing a 45 min. sulfobromophthalein retention of 35% or greater. Unusually severe esophageal bleeding occurred preoperatively in four of the successful operations and required the use of the Sengstaken tube just prior to operation.[3] In two of these the tube was kept in place for three weeks preoperatively.

Several types of shunts between the portal venous system and a systemic vein are effective. Each has advantages, and we believe that no one procedure should be championed as the one of choice. The end-to-side splenorenal anastomosis has the advantage of being unaffected by the masses of veins which are often present in the hepatoduodenal ligament. The common bile duct and the hepatic artery are not endangered in its accomplishment. Removal of the enlarged spleen and its peripheral blood-cell-depressing effect is also advantageous. The hazard of mesenteric thrombosis is, theoretically at least, minimized.

3. Sengstaken, R. W., and Blakemore, A. H.: Balloon Tamponage for the Control of Hemorrhage from Esophageal Varices, Ann. Surg. **131**:781-789, 1950.

The end-to-side portal vein to vena cava shunt, which is without doubt the most effective in decompressing the portal bed, deprives the liver of all portal vein blood. The disadvantage mentioned by several surgeons, including one of us,[1k] namely, that complete portal vein obstruction is necessary during the production of the shunt may be overemphasized. The long-continued portal obstruction has prepared the system for such a procedure just as a coarctation of the aorta makes possible the obstruction of the vessel during repair.

Side-to-side portacaval anastomosis has the advantage of permitting direct portal vein decompression without even temporarily interrupting the flow into the liver. The only serious disadvantage lies in the frequency of closure of experimental fistulas of this type.

We suspect that a large factor in the choice of procedure is the previous experience of the surgeon with the various operations. Our experiences have led to a preference for splenorenal anastomosis unless a distinct indication for another is present.

In this series a splenorenal anastomosis was used in 18 cases and a portacaval in three. All splenorenal anastomoses were end-to-side between the splenic and left renal veins. A thoracoabdominal incision, the technique of which has been described previously, was used.[4] Of the three portacaval anastomoses, a direct side-to-side shunt was done in two and in one an indirect communication was formed, using a vein graft between the portal vein and the vena cava. A shunt could not be completed in the six unsuccessful cases for various reasons including excessive bleeding at operation due to large collaterals in the hepatoduodenal ligament, a totally obliterated portal vein in one patient who had undergone a splenectomy, and such factors as shock and extended operative time in three older patients. The drop in portal system pressure has been most striking after splenorenal anastomosis. This pressure has not always been measured because of the hazard of inserting the needle into the splenic vein. The observation of rapid turbulent flow from splenic vein to renal vein and the collapse of the splenic vein in size and turgidity has been considered ample evidence of good decompression.

Measurement has been made of the splenic vein pressure before and after ligation of the splenic artery with the spleen in place in eight patients (Table 1), to provide some objective data pertaining to the possible value of splenic artery ligation alone in portal hypertension. In none of these patients has there been a significant immediate drop in the splenic vein pressure. The criticism of these observations is the comparatively short time allowed after ligation of the artery before the second pressure readings were taken. It may be that during this period an insufficient volume of portal system blood drains away to allow the obstruction of splenic artery inflow to become effective. Clinically, Everson and Cole [5] and others [6] have reduced temporarily the tendency for esophageal bleeding by splenic artery ligation.

4. Julian, O. C., and Fildes, C. E.: Shunt Operations for Esophageal Varices, S. Clin. North America **31**:229-258, 1951.

5. Everson, T. C., and Cole, W. H.: Ligation of Splenic Artery in Patients with Portal Hypertension, Arch. Surg. **56**:153-160 (Feb.) 1948.

6. Blain, A. W.: Ligation of Splenic Artery, Surg., Gynec. & Obst. **26**:660-662 (June) 1918. Watson, R. B.: Ligation of Splenic Artery for Advanced Splenic Anemia, Brit. M. J. **1**:821, 1935. Blain, A. W., and Blain, A., III: Ligation of Splenic Artery, Operation of Choice in Selected Cases of Portal Hypertension and Banti's Syndrome, Ann. Surg. **1**:92-99, 1950. Berg, A. A., and Rosenthal, N.: Ligation of Splenic Artery for Thrombocytopenic Purpura and Congestive Splenomegaly, J. Mt. Sinai Hosp. **8**:382-398, 1942.

Postoperative complications have been common but rarely serious. Five patients required aspiration of pleural effusions. Empyema occurred in two cases; in one it followed a rupture of the suture line in the diaphragm, with perforation of the stomach. This complication was followed by recovery after reoperation for closure of the perforation.

An analysis of the mortality (Table 2) shows that there has been one postoperative death and two subsequent deaths in the series of patients on whom a successful shunt was performed. The three deaths occurred in patients who showed

TABLE 1.—*Effect of Obstruction of Splenic Artery on Splenic Vein Pressure*

Case No.	Splenic Vein Pressure, Mm. of Water	
	Initial	After Clamping Artery
5	245	240
7	200	280
9	220	210
10	320	310
11	220	210
12	220	210
13	238	234
14	280	240

TABLE 2.—*Analysis of Mortality*

	No.	Time	Cause
Completed portacaval shunts	0	.....	.....
Completed splenorenal anastomosis	3	7 days	Liver failure
	..	4 mo.	Progressive liver failure
	..	4 mo.	Acute hepatitis after recovery
Failure to complete anastomosis	3	24 hr.	Esophageal and wound bleeding
	..	3 wk.	Liver failure, mesenteric vein thrombosis
	..	2 mo.	Acute hepatitis after recovery

TABLE 3.—*Summary of Shunt Operations*

	No.	Surgical Mortality		Subsequent Mortality		Recurrence of Bleeding, No.
		No.	%	No.	%	
Splenorenal anastomosis	18	1 (7 days)	3.7	2 (4 mo.)	7.3	0
Portacaval anastomosis	3	0	...	.....	...	1
Uncompleted cases	0	1 (24 hr.)	7.3	1 (2 mo.)	3.7	2
Totals	27	3	11	3	11	3
Over-All Mortality			22%			

severe preoperative liver dysfunction manifested by sulfobromophthalein retention of 35% or more plus low serum albumin values. These patients were selected for operation because it was considered that their severe bleeding represented a greater danger than did the liver disease. One of the deaths was in a patient whose shunt was estimated at the time of operation to have been technically poor. At the time of autopsy, four months postoperatively, the anastomosis in this man was found to be closed. Autopsy in the remaining two cases disclosed a wide open anastomosis at one week and four months, respectively (Figs. 1 and 2).

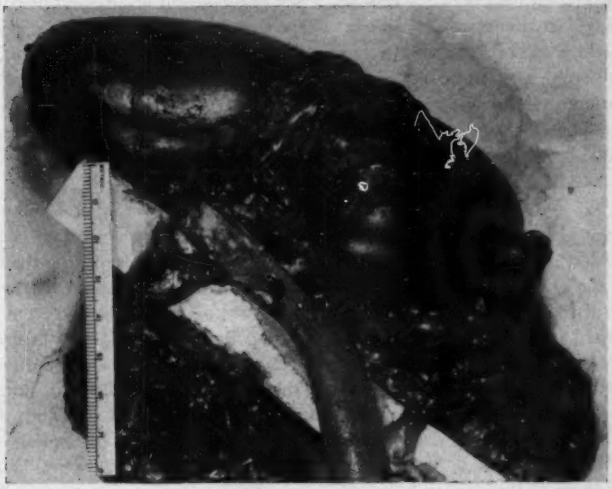

Fig. 1.—Autopsy specimen of splenorenal anastomosis four months postoperatively. Renal vein and splenic vein under pressure from saline in syringe.

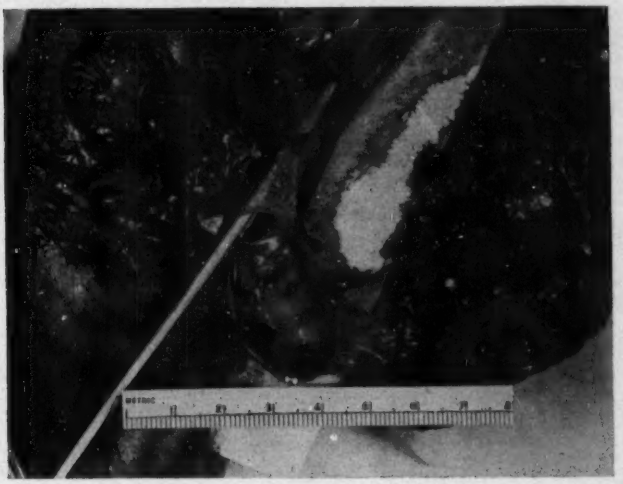

Fig. 2—Opened splenorenal anastomosis showing suture line and patency of shunt.

Eighteen living patients who underwent a successful shunt operation have been followed for two to 30 mo. (Table 3). Only one has had esophageal bleeding postoperatively. In this instance a lateral portacaval anastomosis had been performed. One patient with severe ascites preoperatively has had disappearance of ascites since his splenorenal anastomosis. Liver function has not been significantly affected in these patients. Follow-up esophagoscopy has not yet been done in all patients. In those in which it has been completed a distinct tendency to shrinkage of varices has been shown, and in two there has been a complete disappearance.

COMMENT

Venous shunt operations have as their sole indication the reduction of portal hypertension for the purpose of diminishing the tendency to bleed from the collateral veins of the upper gastrointestinal tract. Selection for operation on the basis of an estimate of the comparative danger to the patient of liver dysfunction and bleeding has resulted in this series in three deaths from liver failure. Relief of ascites has been a distinct result in one patient. There has been no evidence of improvement in liver function following decompression of the portal system. There is, however, an indirect advantage to the liver in preventing repeated hemorrhages and, therefore, periods of relative anoxemia of the liver cells. The results in prevention of recurrence of hemorrhage have been encouraging. The period of follow-up, however, is just beginning to be adequate.

SUMMARY

Twenty-seven patients with portal hypertension have been operated on for the production of a venous shunt. Eighteen splenorenal anastomoses and three portacaval shunts, one through a vein transplant, have been completed. Relief of bleeding has been complete in 17 patients during a follow-up period of two to 30 mo. The effect of ligation of the splenic artery on portal pressure has been studied in eight patients. No significant drop in venous pressure has occurred.

LIGATION OF HEPATIC AND SPLENIC ARTERIES IN TREATMENT OF PORTAL HYPERTENSION

Ligation in Atrophic Cirrhosis of the Liver

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IN A PREVIOUS communication [1] we reviewed the clinical causes and the present-day methods of treatment of portal hypertension. We also discussed the physiology of the hepatic circulation, and one of us (J. K. B.) presented the results of experimental work on portal hypertension since March, 1947. This work may be summarized briefly as follows:

I. Survival After Ligation of Hepatic Artery
   A. Without preparation with penicillin and streptomycin
      1. Ligation close to liver caused death due to liver necrosis and gangrene of gall bladder with bile peritonitis
      2. Ligation at source caused death due to liver necrosis and gangrene of gall bladder, with bile peritonitis in many instances
   B. Preparation with penicillin and streptomycin
      1. Ligation close to liver caused death due to liver necrosis
      2. Ligation at source resulted in survival if dogs were cared for properly

II. Collateral Circulation After Ligation of Hepatic Artery at Source
   A. Injection of iodopyracet (diodrast®) through catheter introduced into right common carotid artery down to celiac axis
      1. Prodigious collateral circulation demonstrated
   B. Injection directly into aorta above the inferior mesenteric artery with temporary ligature below the site of injection
      1. Extensive collateral circulation demonstrated
   C. Injection of dicetyl phosphate in olive oil into the hepatic artery before ligation caused death due to hepatic insufficiency within a few hours; one month after ligation injection of the same substance into a collateral channel did not cause death of animal

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This study was supported by a grant from the Charles J. Wolf Foundation for Medical Research. The Lilly Research Laboratories provided many facilities for these experiments.

1. Berman, J. K.; Koenig, H., and Saint, W. K.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension, Quart. Bull. Indiana Univ. M. Center **12**: 99, 1950.

III. Effect of Ligation of Hepatic Artery at Celiac Axis on Portal Venous Pressure

A. A fall in pressure of 10 to 20 mm. of water resulted

B. Systemic arterial pressure remained constant as shown by simultaneous recordings from femoral artery

IV. Effects of Ligations of Hepatic and Splenic Arteries on Portal Venous Pressure

A. Ligation of splenic artery after the hepatic artery was tied caused an additional drop in portal venous pressure of 40 to 50 mm. of water

1. Systemic arterial pressure remained constant

B. Ligation of splenic artery first caused a slight fall in portal venous pressure equal to 5 to 10 mm. of water; after hepatic artery ligation there was an additional fall of 40 to 60 mm. of water

C. Ligation of the hepatic artery and then of the splenic artery one month later caused an additional fall in portal pressure; if the splenic artery was tied first, then the hepatic artery 30 days later, there was a precipitous fall in portal pressure

D. Ligation of the celiac axis produced a fall in portal pressure of 40 to 60 mm. of water

1. Apparently the occlusion of the left gastric artery did not affect portal venous pressure because when tied alone no change occurred

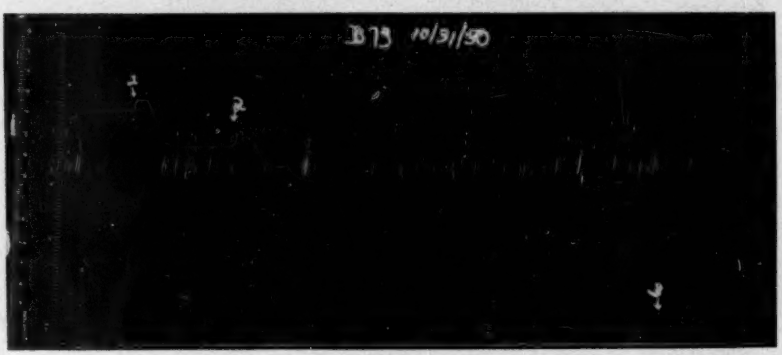

Fig. 1.—Kymographic tracing to show the effect of ligation of the splenic and hepatic arteries: 1. Ligation of the splenic artery. There is a fall in portal pressure from 115 to 96 mm. of water.

2. Ligation of the hepatic artery. A precipitous fall is shown to 6 mm. of water.

3. The spleen was removed at this point. This produced a slight fall followed by a rise in portal pressure.

E. Splenectomy caused first a slight added fall in portal pressure for about 20 min., then a rise slightly above that which occurs without splenectomy (Fig. 1)

V. Effects of Ligation of Hepatic and Splenic Arteries After Attempts to Produce Portal Hypertension

A. Injection of dicetyl phosphate around portal vein caused enormous fibroplasia; after 30 to 60 days collaterals appeared in gastrohepatic ligament; portal venous pressures were only slightly higher

1. Ligation of hepatic and splenic arteries produced a fall in portal venous pressures of 30 to 40 mm. of water

B. Injection of dicetyl phosphate around the inferior vena cava above the diaphragm produced a slight rise in portal venous pressure after 30 days; ascites developed in 60 to 90 days but disappeared within six months

1. Effects of hepatic and splenic artery ligation were the same as in *A*

C. Partial ligation of the inferior vena cava above the diaphragm with polythene film produced a greater rise in portal venous pressure than in *B*; a large amount of ascites developed in 60 to 90 days and continued to form in spite of paracenteses

1. Results of hepatic and splenic artery ligations were the same as in *A* and *B*; ascites gradually disappeared in two to three months

VI. Effects of Ligation of Hepatic and Splenic Arteries After Attempts to Reduce Portal Pressure by Portacaval Shunts

A. Side-to-side portacaval anastomosis before ligation of the hepatic and splenic arteries did not change the results; the average pressure in three dogs prior to the creation of a shunt was 130 mm. of water; after completion of the shunt it was 65 mm. of water, and following hepatic and splenic artery ligation it was 20 mm. of water; ligation of the portal vein on the hepatic side of the portacaval shunt caused a transient rise in portal pressures followed by a fall greater than in *A*, *B*, or *C* of Part V; many of the dogs in which the portal vein was tied died within 48 to 72 hr. because of a thrombosis at the site of the shunt; this resulted from the low pressure in the portal vein after hepatic and splenic artery ligation

Conclusions.—Experiments on dogs seem to indicate that ligation of the hepatic and splenic arteries will produce a sustained fall in portal venous pressure and may be applicable in the treatment of portal hypertension.

The results of our experiments may be explained on the basis of extensive studies on human normal and cirrhotic livers by various observers.[2]

Fig. 2.—Kymographic tracing to show the effect of ligation of the splenic and hepatic arteries. An 18-gage needle was inserted into the portal vein, and a cannula was placed in the femoral artery. The first drop in portal pressure followed ligation of the hepatic artery. The second resulted from splenic artery ligation. The femoral artery pressure was not affected.

STUDIES ON THE NORMAL CIRCULATION IN THE LIVER

The liver is a vascular unit with two large venous vascular beds dovetailing into each other in such a way that no two vessels come in contact and all terminals are at a distance from each other. The intervening space is occupied by hepatic cells, so that a maximal amount of portal blood in its path to the hepatic vein is exposed to as much parenchyma and for as long as possible. The central veins receive their tributary sinusoids from the parenchyma throughout their whole length; the portal veins give off their sinusoids only from their extreme tips. The hepatic vein runs alone and is surrounded by parenchyma throughout its course with the intervention of a small amount of perivascular connective tissue, an exten-

2. (*a*) Herrick, F. C.: An Experimental Study into the Cause of the Increased Portal Pressure in Portal Cirrhosis, J. Exper. Med. **9**:93, 1907. (*b*) McIndoe, A. H.: Vascular Lesions of Portal Cirrhosis, Arch. Path. **5**:23 (Jan.) 1928. (*c*) Dock, W.: Role of Increased Hepatic Arterial Flow in Portal Hypertension of Cirrhosis, Tr. A. Am. Physicians **57**:302, 1942.

sion of the fibrous tissue of the portal spaces. There is no anastomosis either with the portal vein or with the hepatic artery except through the sinusoidal bed, and the two venous systems are always separated by parenchyma. In 1873 Gad [3] wrote a dissertation, based upon experimental work, in which he concluded that the arterial circulation of the liver performed a double function in that it brought oxygen to the liver and mechanically controlled the portal flow. He found by experiments with rabbit livers that a current through the arteries retarded portal flow.

In investigation of the functions of the liver, the important fact to remember is that a study of the blood flow through this organ is probably the most significant consideration if a proper understanding of the disease process in portal cirrhosis

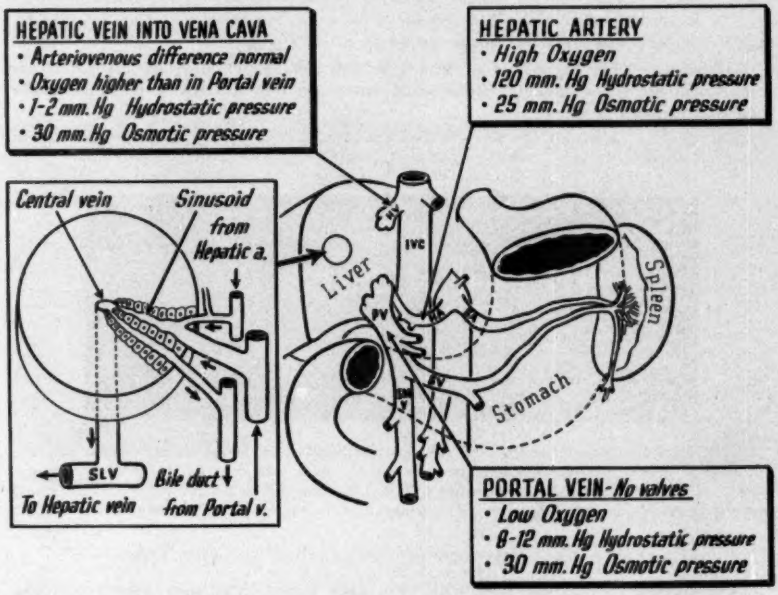

Fig. 3.—Diagram illustrating normal circulation of the liver. *SLV* indicates sublobular vein; *IVC*, inferior vena cava; *SMV*, superior mesenteric vein.

is to be obtained. The hepatic artery has a very small volume circulation with a high pressure, while the portal vein has a large volume circulation with a low pressure. There is a common channel of exit for blood entering these two circulations. Furthermore, the circulations lie in an expansible tissue framework, and all circulations influence each other either by direct communication or by lateral pressure.[4] All observers are agreed that the freely expansible tissue framework is

3. Gad, cited by Herrick.[2a]

4. Bradley, S. E.: Variations in Hepatic Blood Flow in Man During Health and Disease, New England J. Med. **240**: 456, 1949.

perhaps the most important factor toward maintaining the proper balance between the portal circulation and the hepatic artery circulation. This is true because the hepatic artery has a pressure roughly of 120 to 130 mm. Hg and the portal vein roughly of 8 to 12 mm. Hg, but these different pressures come to a common level at the junction of their interlobular or intralobular branches. The third component in this pressure system is the hepatic vein, which is a separate unit without the free communication that exists between the hepatic artery and the portal vein. The pressure within the hepatic vein varies greatly but is roughly 1 to 2 mm. Hg. We know that the pressure must be higher than that in the inferior vena cava, which varies with respiration and is about 0.5 mm. Hg below the diaphragm and about 10 mm. of water above the diaphragm; it is still positive as compared with the intrathoracic pressure, which varies from —2 to —5 mm. Hg. At the level of the right atrium the pressure in the vena cava is approximately 5 mm. of water. The osmotic pressure in the portal vein is higher than the osmotic pressure in the hepatic artery. In the hepatic artery osmotic pressure is about 25 mm. Hg, while in the portal vein it is 27 to 30 mm. Hg. The osmotic pressure within the hepatic vein is probably 27 to 28 mm. Hg. Thus, the hydrostatic pressure of the portal vein is low and the osmotic pressure is high, favoring the rapid absorption of solutes into the portal system (Fig. 3).

STUDIES ON THE PRESSURE RELATIONSHIPS OF THE PORTAL VEIN, HEPATIC ARTERY, AND HEPATIC VEIN BY PERFUSION EXPERIMENTS

Experimental work on the human liver by perfusion was first done by Herrick [2a] in 1907. These experiments on the normal and cirrhotic liver were repeated by McIndoe [2b] in 1928 and by Dock [2c] in 1942. Herrick's work clearly shows that in the normal liver there is a rise in portal pressure of 1 mm. Hg for every 40 mm. Hg of arterial pressure. In the cirrhotic liver the rise was 1 mm. for every 6 mm. of arterial pressure. If this experiment was reversed and if the arterial pressure was set at, say, 130 mm. Hg, it was found that for every 7 mm. increase in the portal pressure the arterial rise was 1 mm. Hg. However, in the cirrhotic liver there was a rise in arterial pressure of 1 mm. Hg for every 3 mm. increase in the portal pressure. In the normal liver there is a perfectly balanced point of pressure which is disturbed in the cirrhotic liver, causing a freer communication of the arterial with the portal vessels.

Gad [3] described the arterial branches uniting with the portal venules at an acute angle, leaving a wedge-shaped valve between them. With a like pressure in the portal vein and the hepatic arterial components, there would be a free flow through both, but if the pressure of either was increased there would be a narrowing of the other's lumen and a reduction in its flow. Since the artery component is small and the vein is large, it can be readily seen that a proportionate increase on the portal vein side could easily occlude the hepatic arterial branches, whereas the reverse could not be true because of the size of the portal diameter. Moreover, if there is no arterial flow, it is evident that the large portal volume will entirely occlude the entering arterial capillaries, and fluid cannot flow back through them. When, on the other hand, there is no portal flow and there is a flow through the arteries, their channels being of much smaller size than the portal veins they are unable to occlude the portal vessels and, therefore, the fluid returns through them. However, the

arterial components do offer some resistance to the portal flow. In the normal liver, in order to overcome arterial resistance to the portal flow, the portal pressure must be raised above 10 mm. Hg. But in the cirrhotic liver the portal pressure necessary to resist 130 mm. of arterial pressure is much higher, being 40 mm. Hg.

McIndoe's beautiful specimens of the injected cirrhotic liver show that the tiny portal veins are distorted and twisted, curled on themselves, and finally broken up into a network of stunted venules. The same changes are present in the tree of the hepatic veins and the hepatic artery. However, the most pronounced changes are in the portal and hepatic veins. The terminals of the two systems no longer alternate with one another but tend to lie together and to assume a basket-like arrangement. The central veins are pushed to the periphery of the lobule and, finally, lie next to the portal vein. The collaterals from the portal veins arise before their terminals are reached. The hepatic cells are thus divorced from their blood supply. Portal blood is diverted to collaterals first, and, therefore, the hepatic artery remains as the sole source of nutrition to the cirrhotic liver. McIndoe further showed that, at 20 mm. Hg pressure in the portal vein of the cirrhotic liver, 87 to 100% of a perfusion fluid passes directly into the collateral circulation and only 13% at most, is recovered from the hepatic vein; since the collaterals are given off before the sinusoidal bed is reached, none of the fluid, or very little, comes into contact with liver cells. In cirrhosis a spontaneous Eck fistula develops between the portal vein and the vena cava. The hepatic veins are bypassed and nourishment depends upon the hepatic artery. Hepatic insufficiency in cirrhosis then is an expression of vascular deficiency rather than a deficiency of the liver cell, because it has been shown by Mann [5] and others that the liver cell regenerates very easily and even two-thirds of the liver may be removed with complete regeneration. In cirrhosis there is a dissociation between portal and hepatic venous radicles; then collaterals form between the portal vein and the vena cava which shunt 87 to 100% of the portal blood. Moschcowitz [6] describes what he terms angiogenesis in the liver establishing a shunt between the portal and hepatic vein to compensate for the distortion and narrowing of the liver's vascular content—in other words, an intrahepatic Eck fistula. A similar situation was demonstrated by us after slow occlusion of the portal vein.[1]

The hepatic artery sends blood into the portal as well as the hepatic vein, but in both instances there is what amounts to a shunt from artery to vein without nourishment of the liver cell. Sabourin,[7] as early as 1885, showed that an intrahepatic collateral circulation was formed between the hepatic artery and the portal vein in Laennec's cirrhosis. This has been confirmed by Epplen [8] and others.[9] Therefore, we have a situation which is comparable to a cavernous hemangioma,

5. Mann, F. C.: The Effects of Complete and Partial Removal of the Liver, Medicine **6**: 419, 1927.

6. Moschcowitz, E.: Laennec Cirrhosis: Its Histiogenesis, with Special Reference to the Role of Angiogenesis, Arch. Path. **45**: 187 (Feb.) 1948.

7. Sabourin, C.: Recherches sur l'anatomie normale et pathologique de la glande biliare de l'homme, Paris, F. Alcan, 1885; cited by Moschcowitz.[6]

8. Epplen, F.: Pathology of Cirrhosis of the Liver: An Historic Pathologic Study, Arch. Int. Med. **29**: 482 (April) 1922.

9. Popper, H.; Waldstein, S. S., and Szanto, P. B.: Correlation of Clinical Features of Cirrhosis of the Liver with Findings of Biopsy, Am. J. Clin. Path. **20**: 724, 1950.

or an arteriovenous varix with a high arterial pressure which is communicated directly to the veins and which retards outflow from the veins, much as in the abnormal arteriovenous communication of the cirrhotic liver (Fig. 4).

In 1942 Dock used kerosene instead of saline solution as perfusing liquid. He studied the total flow of the normal and the cirrhotic liver with portal pressure at 20 mm. Hg and arterial pressure at 0; with arterial hepatic pressure at 100 mm. Hg and portal pressure at 0 and with arterial hepatic pressure at 100 mm. Hg and portal pressure at 20 mm. Hg. The decrease in portal flow on opening the arterial trunk at 100 mm. Hg was 30% in normal livers, 28% in livers showing nonalcoholic cirrhosis, and 78% in livers exhibiting alcoholic cirrhosis. Thus, a rise in pressure greatly above 20 mm. Hg is necessary to restore normal portal

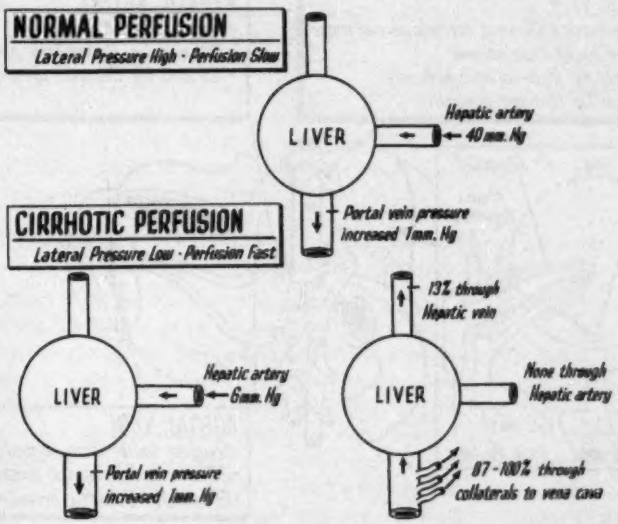

Fig. 4.—Diagram of perfusion experiments.

hepatic flow. There is a diminished total flow in cirrhosis which may equal one-fifth of the normal. In atrophic cirrhosis the portal hypertension is severer than it would be if the arterial inflow were reduced. In acute alcoholic cirrhosis with a large fatty liver, the sinusoids are blocked by extrinsic pressure producing portal obstruction, but there is no portal hypertension. This fact lends credence to the role of the hepatic artery in the production of portal hypertension in the fibrotic liver. Dock concluded that there was some damage at the arterial-portal anastomosis to account for the change.

From a review of the evidence on perfusion experiments, we must conclude that there is a close relationship among pressures in the portal branches, the hepatic arterial vessels, and the hepatic venous system. The last is affected also by caval pressures, as seen in cardiac failure. The more blood that is shunted into the vena

cava, the higher its pressure may be, thereby interfering with hepatic venous return. Therefore, we must assume that the liver depends upon a relationship among the various pressures. The effects of varying pressures among the three principal vessels are more exaggerated in the cirrhotic than in the normal liver.

PROBABLE SEQUENCE OF EVENTS IN CIRRHOSIS

The morbid changes in cirrhosis seem to occur as follows:

1. There is a dissociation between the portal and the hepatic venous systems. As a result of this dissociation, the free exit of blood from the portal sinusoids into the central vein is delimited.

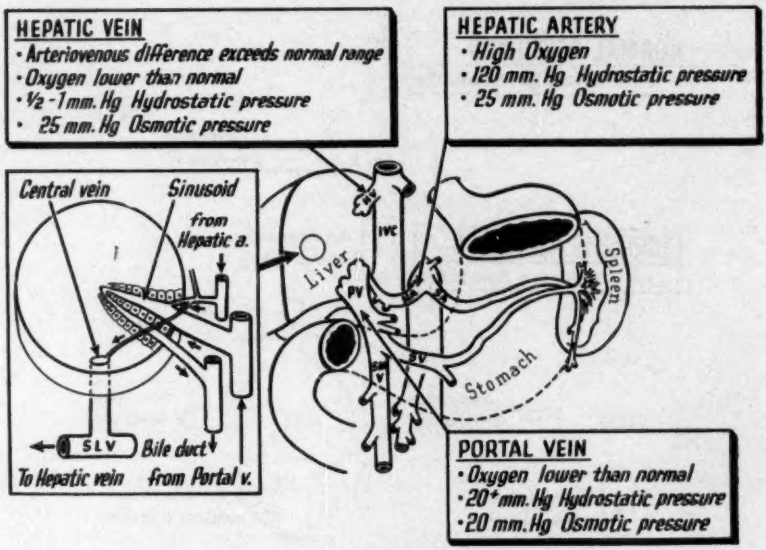

Fig. 5.—Diagrammatic illustration of the probable changes in the circulation of the cirrhotic liver. The arteriovenous difference exceeds the normal range,[4] but this may be attributed to the stagnant anoxemia caused by the large hepatic venous collateral bed.

2. With this dissociation portal pressure increases, and a more direct communication results between the hepatic artery and the portal vein branches.

3. Portal pressure rises, and collaterals form before the sinusoidal bed is reached. These collaterals are between the portal and the systemic venous systems and occur, as is well known, in the various venous beds in the abdomen, which are seen clinically as esophageal varices, hemorrhoids, and enlarged veins on the abdomen, in the gastrohepatic omentum, and elsewhere. The increased hydrostatic pressure within the portal vein is accompanied with a decrease in the osmotic pressure, owing to the fact that the patient does not ingest sufficient protein and the liver fails to produce an adequate quantity of serum albumin. In addition, the

oxygen content of the portal vein is decreased because of stagnant anoxemia within the portal system. These three factors are probably responsible in great measure for the ascites which usually ensues. The decreased osmotic pressure is perpetuated by the continued loss of albumin into the ascitic fluid.

4. The collaterals shunt 87 to 100% of the portal blood into the systemic venous circulation.

5. The hepatic artery continues to supply blood to the liver and is, in fact, the only source of supply when portal obstruction is far advanced because the artery does not partake of the distortion process as quickly as do the venous components. Therefore, for a long time blood is shunted from the hepatic artery to the portal system by way of the sinusoids and into the hepatic veins by arterial collaterals.

6. At this point it would seem that there are two more or less abnormal arteriovenous communications: one from the hepatic artery to the portal vein by way of the sinusoids, and the other from the hepatic artery to the hepatic vein by way of collaterals which occur from newly formed capillaries and also from the connections which are normally present. We are now studying oxygen values in the portal vein and inferior vena cava at the time of operation to obtain more data which might confirm this hypothesis (Fig. 5). Even before this period is reached, the high hepatic artery pressure forces the portal venous pressure to a higher level, as proved by both Dock and Herrick.

RATIONALE FOR LIGATION OF THE HEPATIC AND SPLENIC ARTERIES—HYPOTHETICAL CONSIDERATIONS

Ligation of the hepatic artery may be helpful in the treatment of portal hypertension because it cuts down the pressure within the arterial tree, permitting the portal venous component to enter the sinusoid at a much lower pressure. Moreover, the pressure within the hepatic artery is probably one of the perpetuating forces responsible for the increase in portal venous pressure. The experimental observations which we have cited in our own work and the perfusion experiments of others seem to point to the fact that with the decrease in the arterial pressure the portal pressure will also be decreased and portal blood will flow more freely into the sinusoids than before. This would then act very much as ligation of the arterial component of a cavernous hemangioma and would force arterial collaterals to form which would allow a capillary bed to arise within the liver and thereby permit nourishment to the starved hepatic cells. We demonstrated an increase in collaterals after dividing the hepatic artery by injection of dicetyl phosphate in the distal end of the artery,[1] and also by roentgen examination after the injection of iodopyracet. The same analogy may be carried out as with the cavernous hemangioma or arteriovenous varix in that if the portal volume flow remains the same the lateral pressure within the portal vein may be great enough to occlude the new hepatic arterial capillaries which are trying to form within the liver. This could prevent the formation of a new capillary bed.

If, however, provision is made for a decrease in the volume flow of portal blood until the arterial collaterals can be formed, then "revascularization" may take place. This is accomplished by ligation of the splenic artery, which has the same effect on the spleen as does ligation of the hepatic artery upon the liver; namely, there

is an increase in the lateral pressure proximal to the ligature and the formation of collaterals. In the late stages of portal hypertension the pulp cells of the spleen become predominantly fibroblasts; the sinuses show extensive hyperplasia and become very prominent, producing an angiomatous appearance.[10] The circulation of the spleen is converted from an open to an almost closed one. This seriously compromises the reservoir function of the organ. Therefore, ligation of the splenic artery in patients with splenomegaly is a logical procedure because it permits collaterals to form in the pulp, thereby restoring the spleen's ability to hold blood. It is also useful in cirrhotic patients without splenomegaly because it increases the storage space of the organ. The immediate effect of splenic artery ligation is a decrease in the size of the organ. After collaterals form, the spleen increases in size.

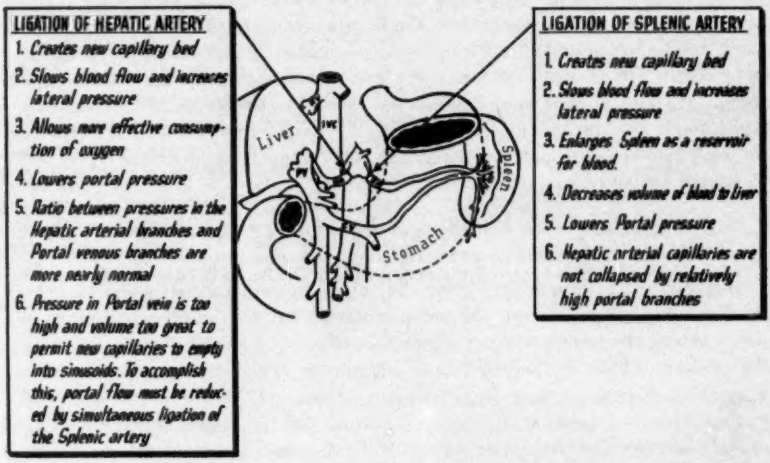
LIGATION OF HEPATIC ARTERY
1. Creates new capillary bed
2. Slows blood flow and increases lateral pressure
3. Allows more effective consumption of oxygen
4. Lowers portal pressure
5. Ratio between pressures in the Hepatic arterial branches and Portal venous branches are more nearly normal
6. Pressure in Portal vein is too high and volume too great to permit new capillaries to empty into sinusoids. To accomplish this, portal flow must be reduced by simultaneous ligation of the Splenic artery
Liver
IVC
Spleen
Stomach
LIGATION OF SPLENIC ARTERY
1. Creates new capillary bed
2. Slows blood flow and increases lateral pressure
3. Enlarges Spleen as a reservoir for blood.
4. Decreases volume of blood to liver
5. Lowers Portal pressure
6. Hepatic arterial capillaries are not collapsed by relatively high portal branches

Fig. 6.—Diagram illustrating the possible effects of ligation of the hepatic and splenic arteries in the treatment of portal hypertension due to atrophic cirrhosis of the liver.

Since 25 to 40% of the portal volume comes from the spleen, occlusion of its artery has a considerable effect in reducing the volume of blood which may reach the liver per minute circulation time. If this procedure acts in a way that might induce hypersplenism, splenectomy may be done later. However, experiments seem to show that reducing the portal vascular bed by splenectomy increases to some extent portal venous pressure. Clinically, splenomegaly is regarded as an unfavorable accompaniment of cirrhosis. This may be explained on the basis that the spleen has reached its storage capacity and is of no aid in diminishing the volume of blood reaching the liver (Fig. 6).

10. Moschcowitz, E.: The Pathogenesis of Splenomegaly in Hypertension of the Portal Circulation: "Congestive Splenomegaly," Medicine **27**: 187, 1948.

EFFECTS ON LIVER TISSUE OF THE OPERATION OF HEPATIC AND SPLENIC ARTERY LIGATION

Our studies seem to show that liver tissue is not damaged by arterial ligation, provided it is done close to the source of supply. The effect on the cirrhotic liver will be determined later after sufficient time has elapsed in our studies on human beings.

SUMMARY

From our observations on animals and man the operation of ligation of the hepatic and splenic artery seems to be a rational procedure in the treatment of certain forms of cirrhosis of the liver—particularly, the atrophic variety. This operation has been carried out in ten patients with advanced cirrhosis of the liver, ascites, and esophageal varices with favorable results, although the time since operation has been too short and the number of cases too few for definite conclusions concerning the effectiveness of this procedure.

DISCUSSION

Dr. John H. Grindlay, Rochester, Minn.: The primary hypothesis on which Dr. Berman has based ligation of the hepatic artery in treatment of cirrhosis of the liver stimulates thought. Experience will sooner or later show whether the hypothesis is correct, partly right, or useful mainly because it has stimulated us. In its simplest form, the hypothesis is that improvement of the cirrhotic liver might be brought about if more portal blood could be made to flow through it. It is as reasonable a hypothesis as the one currently in vogue which holds almost the opposite, that shunting of portal blood into the vena cava and away from the liver does no harm to, or might even help, the cirrhotic liver. The hypothesis which Dr. F. C. Mann, Dr. J. L. Bollman, and I support because of old and recent studies is close to Dr. Berman's; it is that liver regeneration is dependent on a supply of venous, though not necessarily portal, blood.

The secondary hypothesis proposed by Dr. Berman is that arterial flow impedes portal flow where the two systems join together. We hope Dr. Berman and his colleagues will continue their excellent work and determine whether ligation of the hepatic artery is attended by increased rate of portal flow, as well as drop in pressure, and for how long. Also, will ligation of the hepatic artery have the same effect on the cirrhotic as on the normal liver? It is conceivable that the great displacement and disarrangement of portal veins and branches in the liver may be the really significant impediment to portal flow, and that the factor of arterial inflow is insignificant by comparison.

Dr. Berman's method of ligation of the hepatic artery, fortunately, does not deprive the liver entirely of arterial blood. Some blood enters the hepatic artery farther along from collaterals. The liver will not survive if the hepatic artery branches are ligated as they enter the liver. At least, Dr. Mann, Dr. Bollman, and I found this to be true in dogs. We learned also that while use of penicillin might keep dogs alive for days or even three weeks, they died of massive liver necrosis unless the liver received a new arterial supply by way of collaterals, mainly those which are in the diaphragmatic ligaments. We could demonstrate this new arterial supply to the liver when we injected radiopaque material into the aorta.

CLOSTRIDIAL INFECTION AS A CAUSE OF DEATH AFTER LIGATION OF THE HEPATIC ARTERY

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IT HAS been known for many years that complete ligation of the arterial supply to the liver is rapidly fatal in several mammalian species. Autopsy examination of animals which have died in this way always shows massive necrosis of the liver. The mechanism of death and the pathological changes leading to it have never been understood satisfactorily. The view which predominates through the literature is based on the assumption that anemic necrosis and subsequent liver failure constitute the important events in the process.

It is of interest that bacterial infection has been implicated previously as a factor in the cause of death following peritoneal implantation of liver tissue—the so-called in-vivo autolysis of the liver. In 1930 Ellis and Dragstedt [1] isolated an anaerobic bacillus from normal dog liver. They found that fetal liver was harmless when implanted into the peritoneum and correlated this finding with the fact that fetal liver was sterile. Nevertheless, the possibility that ligation of the hepatic arterial supply might enable anaerobic organisms to proliferate in the liver does not appear to have been entertained until 1949. During that year Markowitz, Rappaport, and Scott [2] reported that dogs treated with penicillin survived interruption of the hepatic arterial supply, and they asserted that anaerobic organisms were involved in the classically high mortality of untreated animals. Their work stimulated the investigation reported in this paper.

The present investigation was concerned with the relationship of hepatic necrosis to the natural history of the disease pattern which follows ligation of the hepatic artery in the dog. In addition, we sought more direct confirmation of the part played by bacterial infection. To these ends we obtained serial liver cultures and biopsy specimens by a needle-biopsy technique, combined with serial

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From the Department of Experimental Surgery, McGill University Faculty of Medicine.

This investigation was assisted by a Grant-in-Aid from the National Research Council of Canada.

Read at the Eighth Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

1. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. **20**:8 (Jan.) 1930.

2. Markowitz, J.; Rappaport, A., and Scott, A. C.: Prevention of Liver Necrosis Following Ligation of Hepatic Artery, Proc. Soc. Exper. Biol. & Med. **70**:305, 1949; The Function of the Hepatic Artery in the Dog, Am. J. Digest. Dis. **16**:344, 1949.

blood cultures, from animals submitted to the operation of hepatic arterial ligation. The effects on the disease pattern of succinylsulfathiazole (sulfasuxidine®), penicillin, and aureomycin administration were also studied.

EXPERIMENTAL PROCEDURE

Healthy adult dogs were used in the experiments. The diet of these animals before coming under our control was not known. While in our animal house they were fed raw meat.

A standard operative procedure was developed for the interruption of the hepatic arterial supply. Anesthesia was produced by intravenous administration of pentobarbital (nembutal®) in a dose of 5 grains per pound (0.6 gm. per kilogram) of body weight. The abdomen was shaved, scrubbed with medicinal soft soap and water, and carefully prepared with tincture thimerosal (merthiolate®). Strict sterile technique was enforced throughout the operation. A high right rectus incision was used. Biopsy specimens were taken from the right and left lobes of the liver, the wedge incisions being approximated with mattress sutures. Each biopsy fragment was divided into two pieces, one piece being planted in a culture tube and the other fixed for hisological study. A wide dissection of the hepatic artery was done, exposing its origin from the celiac axis and all its branches and anastomoses. Cotton ligatures were placed upon the main hepatic artery near its origin, upon the gastroduodenal and right gastric arteries, and upon any branches running toward the liver, including the hepatic arteries proper. The segment of artery lying between all these ligatures was resected. No attempt was made to preserve the periarterial sympathetic nerves. It is probable that a large proportion of these nerves was resected along with the arterial segment. Cholecystectomy was performed and the cystic duct checked for bleeding and leakage. The abdomen was closed in layers, using cotton sutures. Drainage of the abdomen was not employed. Control blood cultures were obtained before the operation commenced. Postoperative intervals were measured from the time that ligation of the arteries was completed.

Postoperative studies were undertaken as follows: Blood cultures were taken every hour, sometimes every half-hour, after the ligation of the arteries, up to six hours. Liver biopsy specimens were obtained by puncture every two hours up to six hours. Another blood culture and liver biopsy were performed late in the evening, at about the 11th or 12th postoperative hour. At this time the dogs were usually awake, and a pan of milk was given which they usually took well. When the dog was alive the next morning, specimens of blood and liver were taken again, and daily thereafter in surviving animals. Postmortem examination was done as soon as possible after death; observations reported are based only on autopsies performed almost immediately.

Blood specimens for culture were obtained by venepuncture from the superficial vessels of the limbs. Care was taken against contamination by skin and hair. Limbs were shaved, scrubbed with soap and water, and prepared with tincture thimerosal. One cubic centimeter of blood was drawn and transferred directly to liquid culture mediums. No anticoagulant was used. Needle-biopsy specimens of the liver were obtained by puncture through the skin just below the right costal margin into the right lobe of the liver. Similar careful skin preparation was employed. The needle described by Silverman [3] was selected for obtaining the biopsy specimens. The technique gives a cylinder of liver tissue about 1.5 mm. in diameter and between 1 and 2 cm. in length. The specimens obtained were divided for culture and histological study.

Bacteriological specimens were planted in a stoppered test tube containing 10 cc. of Brewer's thioglycollate medium. The tubes were placed in the incubator for 24 hr. Cultures were then transplanted to two sets of blood-agar meat infusion plates. One set was incubated in aerobic and the other in anaerobic environment. After incubation for 48 hr., smears were made of positive cultures and stained with Gram's stain. A target type of hemolysis typical of Clostridium perfringens (Clostridium welchii) was sometimes observed on the blood plates. More frequently a beta type of hemolysis was seen. Microscopically, a positive culture showed the presence of large, stout bacilli. These bacilli usually retained the Gram stain, but

3. Silverman, I.: A New Biopsy Needle, Am. J. Surg. **40**:671, 1938.

occasionally Gram-negative bacilli of the same structure were present together with Gram-positive bacilli in the same smear. Spore formation was demonstrated very rarely. Cultures which were identified microscopically were transplanted into litmus milk culture medium and incubated anaerobically, giving stormy fermentation with an acid reaction. Identification of bacteria usually was limited to the above procedures. However, several strains from different animals were carried through further tests in an attempt to identify the organism more precisely. The following summarizes the results in each instance: Tests showed acid fermentation to lactose, glucose, sucrose, and maltose, but no reaction to mannose. Hydrogen sulfide and nitrites were produced. The reaction to the indigo test was negative. It was concluded that all the positive cultures showed an organism indistinguishable from Cl. perfringens.

Liver biopsy and autopsy specimens for histological study were fixed in cobalt-formaldehyde solution. Sections were stained with Masson's trichrome, Romanowsky's stains, and hematoxylin and eosin.

EXPERIMENTAL STUDIES

Four groups of animals were studied after the routine operation for the interruption of the hepatic arterial blood supply. Preoperative and postoperative studies, as described above, were essentially identical in each group.

Group I was a control group to which no medicament was given.

Group II was fed succinylsulfathiazole by mouth in a dose of 2 grains per pound (0.24 gm. per kilogram) of body weight a day for five days before operation. Stool cultures were done daily from material obtained by rectal swab. *p*-Aminobenzoic acid in a concentration of 0.5 mg. per hundred cubic centimeters was added to all culture mediums used for this group.

Group III was treated with penicillin procaine by intramuscular injection. A standard dose of 300,000 units was used. Penicillinase in a concentration of 1 : 100 was added to the culture mediums.

Group IV received aureomycin [4] by intravenous injection, beginning immediately at the close of the operation. Twenty-five milligrams per kilogram of body weight a day was given in three or four divided doses. Each dog received this therapy two days.

Group V served to confirm the presence of an anaerobic bacillus as a normal contaminant of the livers of the dogs at our disposal. A series of healthy dogs was submitted to lobectomy of the left lobe of the liver under pentobarbital anesthesia and aseptic technique. All animals survived the operation and lived normally. Large pieces of this lobe, more than 25 gm. at a time, were planted in Brewer's medium in 100-cc. flasks, and the cultures were studied as already described.

RESULTS

Group I.—Thirteen control animals were used. The first four dogs operated on served to establish the standard operation described above, and in these animals the postoperative studies were not done. The remaining nine were subjected to the full study program. The first dog of the 13 survived, and on reexploration some weeks later a competent anastomosis through the right gastric artery was found. With this exception the mortality was 100%

The clinical course of the animals was very consistent. After about five hours they usually were walking around and did not appear particularly ill. After a variable period of several hours their condition deteriorated quite suddenly, and death was preceded by a comatose state of short duration. Convulsions were not observed. The time of survival of the eight dogs which died during the autumn was between 16 and 24 hr. The four animals operated on during the spring lived one to four days.

4. Aureomycin used in this study was supplied by the Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

The blood cultures taken just before operation yielded no organisms in any case, but the postoperative blood cultures furnished most striking results. In the nine consecutive dogs so studied, blood cultures became positive at the second or third hour after operation. In every instance pure cultures were obtained of the clostridial organism which could not be distinguished from Cl. perfringens. Once a positive culture was obtained from the blood stream, subsequent cultures remained positive until death.

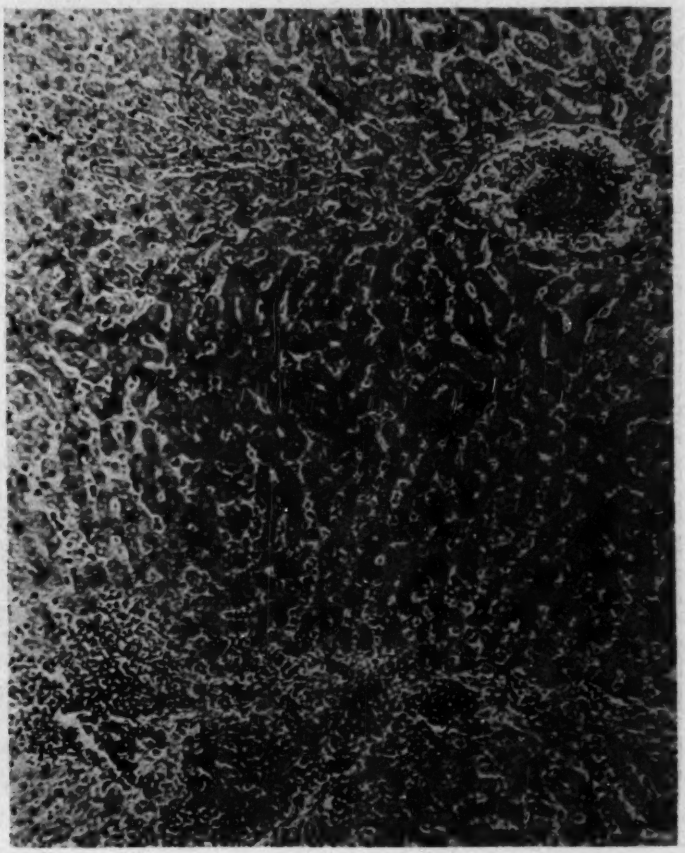

Fig. 1.—Congestion of portal veins with mild congestion of sinusoids but essentially normal parenchyma.

Cultures of the liver biopsy specimens taken at the time of operation gave no growth except in two cases, in which both right and left lobes yielded pure cultures of Cl. perfringens. Postoperatively, positive cultures of this organism were obtained from the needle-biopsy specimens at the third or fourth hour and persisted until death.

Microscopic observations on the specimens of liver changed very little at the intervals studied. Control biopsy specimens taken at operation showed normal liver. No pathological changes of significance were noted in any of the numerous needle-biopsy specimens obtained after operation, with the exception of one case. This animal was already in a moribund state when the needle biopsy was done 11

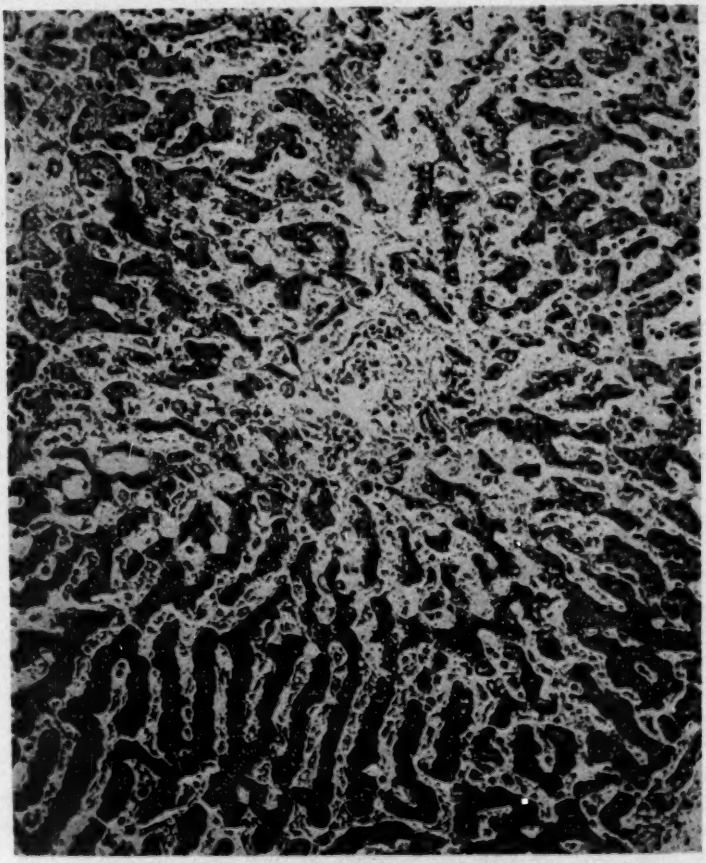

Fig. 2.—Wide distention of sinusoids by edema and debris, including disintegrating red blood cells. Beginning disappearance of hepatic cells around central vein.

hr. after operation. There were slight swelling of the parenchymal cells and alteration of staining properties of both nucleus and cytoplasm. No organisms were seen, nor was there any evidence of definite liver necrosis.

Autopsy observations were essentially uniform. The peritoneal cavity contained 200 or 300 cc. of dark, bloody, foul fluid, which gave pure cultures of Cl. perfringens. The gastrohepatic ligament was examined for the presence of acces-

sory arteries supplying the liver, but none was ever demonstrated; injections were not done. The liver was gray or purple, and crepitation was generally evident, especially in the left lobe. Specimens were taken from right and left lobes for culture and histological study. Cultures were all positive for Cl. perfringens.

Microscopic changes in the liver at autopsy were more extreme in the left lobe than in the right. The lesions were not uniform in either lobe, and areas of severe

Fig. 3.—Area of moderately severe parenchymal involvement, with shrinkage of nuclei and alteration of cytoplasm and some superimposed inflammatory reaction, bordering on an area of massive necrosis with loss of all intracellular detail and some disruption of architecture.

necrosis alternated with areas of mild or minimal involvement. Where involvement was least severe, congestion of portal veins was the salient feature (Fig. 1), with little alteration of the appearance of the parenchymal cells. Elsewhere congestion was more intense and involved the sinusoids, and with disintegration of red blood cells the sinusoids were widely distended with edema and debris (Fig. 2).

Here the parenchymal cells showed swelling, loss of normal details and staining properties of the cytoplasm, and shrinkage and ultimate disappearance of nuclei. In many areas necrosis was extremely severe, with almost complete dissolution of cells and disruption of architecture. Inflammatory response was not a prominent feature where involvement was not severe, being most notable at the periphery of areas of massive necrosis (Fig. 3). Only occasionally was a tendency to abscess

Fig. 4.—Organisms in portal vein, spreading along sinusoids.

formation found. Organisms were seen in large numbers in many areas, chiefly in the portal veins and adjacent sinusoids (Figs. 4 and 5). In some places, well-defined empty ovoid spaces in the tissue were interpreted as gas bubbles produced by the clostridia. The right lobe generally showed a greater proportion of surviving liver tissue than the left; necrosis was more focal in character, and organisms were less numerous.

Group II.—Three dogs were fed succinylsulfathiazole by mouth for five days before operation. Control stool cultures showed the presence of Cl. perfringens,

together with other bacteria. After administration of the drug was started, daily stool cultures showed a decrease in the number of colonies. On the fourth and fifth days, although the stools were not sterile, Cl. perfringens could not be demonstrated.

The clinical course of all three dogs was similar to that of the control group, and they died within 24 hr. Preoperative blood cultures were all negative, and positive cultures appeared two to three hours postoperatively and persisted until

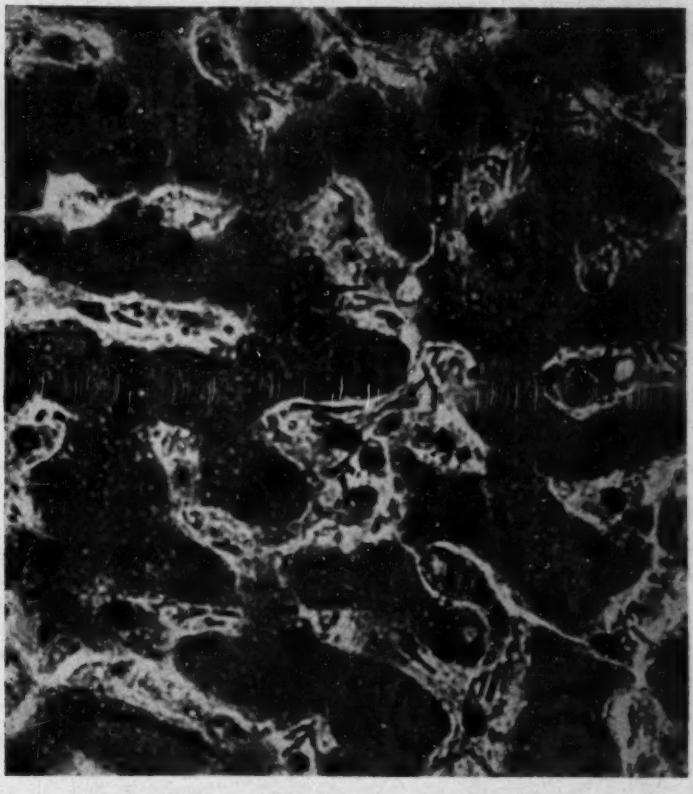

Fig. 5.—Higher magnification, showing large numbers of organisms in sinusoids between relatively undistorted cords of hepatic cells.

death. The same applied to cultures of liver tissue, which first became positive between the fourth and the fifth hours. Histological observations on the liver biopsy specimens, and the autopsy findings, did not differ from those for the control group.

Group III.—Penicillin was administered to nine dogs in various dosage schedules. A single daily injection of 300,000 units was used. Results are summarized

in the Table. It will be seen that in some cases as little as one single dose of penicillin was sufficient protection to permit of indefinite survival. The dogs which survived lived normally after they had recovered from anesthesia. The two which died after the fifth day appeared to have recovered fully but fell ill again on the fourth or fifth day and died. With the exception of one case (Dog 25) the dogs which survived had blood and liver cultures negative for pathogens, while those which died early gave positive cultures from the second hour until death. Dog 20 gave negative cultures for three days and was not followed further. Dog 24 on the third day had negative blood but positive liver culture. Dog 25 was of interest in that blood cultures were positive from the fourth hour to the fourth day and then became negative spontaneously. This dog lived normally for two months and was then killed for examination.

Results of histological studies of the needle-biopsy specimens resembled those of the control group in that nothing remarkable was observed in the liver tissue, whether the animal survived or not. Dogs that died presented findings at autopsy similar to those observed in the control group (Group I). Dogs that survived

Effect of Penicillin Administration on Survival After Deprivation of Arterial Supply

Animal No.	No. of Daily Doses	Time 1st Dose Given	Result	Comment
14	1	Immediately before operation	Died within 24 hr.	Extensive necrosis
15	1	Immediately before operation	Died within 24 hr.	Extensive necrosis
28	1	Immediately after operation	Died within 24 hr.	Extensive necrosis
16	4	1 hr. preoperatively	Survived	Killed; normal liver
18	2	1 hr. preoperatively	Survived	Explored after 4 wk.; liver abscesses
22	1	1 hr. preoperatively	Survived	.....
20	1	1 hr. preoperatively	Died 8th day	Liver necrosis
24	1	1 hr. preoperatively	Died 5th day	Liver necrosis
25	1	1 hr. preoperatively	Survived	Killed; normal liver

were killed two weeks to five months after operation. There was no free fluid or odor. The liver was surrounded by adhesions but was otherwise normal, with one exception (Dog 18). No gross evidence of the establishment of collateral arterial circulation was found, although no injection studies were done. Dog 18 was explored at four weeks and showed several firm nodules in the liver. Microscopically these proved to be well-demarcated abscesses of various sizes (Fig. 6), surrounded by healthy liver tissue; small areas of postnecrotic scarring were also evident. Areas of hyaline degeneration of branches of the portal vein were seen in this specimen.

Group IV.—Aureomycin was administered to two animals, both of which survived and gave completely negative cultures. One died of pneumonia on the 12th day, the right lung being consolidated at autopsy but the liver normal. The other animal was killed at two weeks and showed a small resolving abscess in the left lobe surrounded by healthy liver tissue.

Group V.—Left hepatic lobectomy was performed on nine dogs as described above. The cultures of large pieces of liver were all strongly positive, giving off a pungent odor and large amounts of gas. Cl. perfringens was present in pure culture in every instance. All dogs survived indefinitely.

COMMENT

The results obtained from the control group of animals confirm the fact that death occurs within a short time after the liver is deprived of its arterial supply. The principal finding which we consider to be new is the rapid development of a bacteremia due to Cl. perfringens. This blood-stream infection was demonstrable within two to three hours of the operation and persisted until death. This obser-

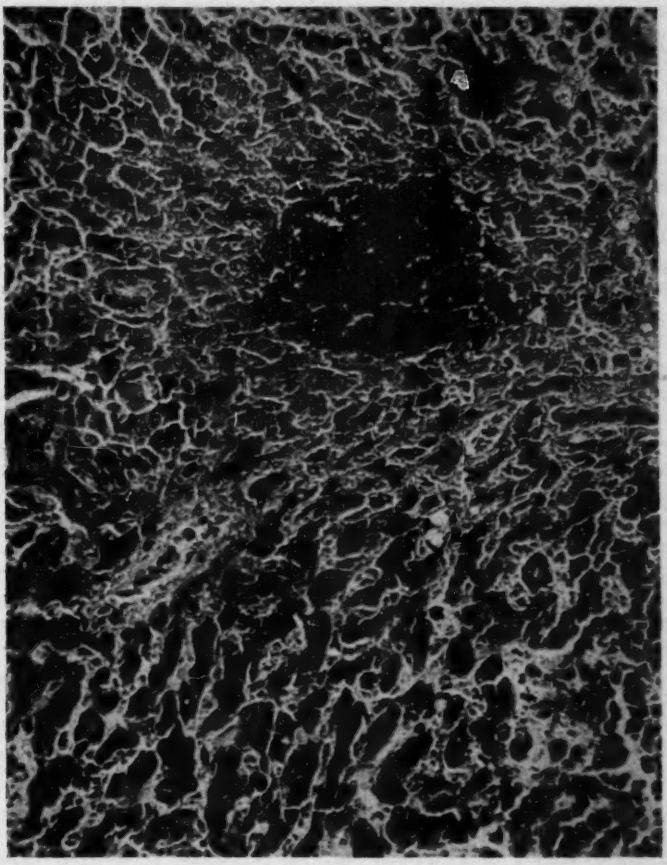

Fig. 6.—Small, well-localized abscess and normal adjacent parenchyma in penicillin-protected dog killed after complete clinical recovery.

vation is complementary to the extensive work of Tanturi, Swigart, and Canepa,[5] who were able to produce a comparable disease pattern by injecting clostridial toxins.

5. Tanturi, C.; Swigart, L. L., and Canepa, J. F.: Prevention of Death from Experimental Ligation of the Liver (Hepatic Proper) Branches of the Hepatic Artery, Surg., Gynec. & Obst. **91**:680, 1950.

Within one or two hours of development of a bacteremia, it was usual to obtain positive cultures of liver tissue. These puncture specimens were taken from the right lobe for technical reasons, although the severest pathological changes always occurred in the left lobe. The puncture specimens were obtained from deep in the substance of the organ. As the liver specimens were unavoidably contaminated with blood presumably already infected, it is perhaps unwise to lay too much stress on selective infection of the liver being present at the early stages. However, the striking fact of the blood-stream infection appears to be well established.

The question arose whether the severe infectious necrosis in the liver originated from organisms already present in the organ, or whether they made their way into the liver from the intestinal tract after the establishment of relatively anaerobic conditions by the removal of the hepatic arterial supply. The experimental group fed succinylsulfathiazole preoperatively (Group II) was planned to test the latter possibility. The results failed to show any degree of protection whatever, despite cultural evidence from the bowel that the clostridia were markedly suppressed. The behavior of the animals in this group was identical with that of the controls in regard to clinical course, postoperative cultures, and autopsy findings.

In the liver-culture group (Group V), the left lobe of the liver was removed from apparently healthy dogs and large masses cultured with uniformly positive results. This suggests strongly that the animals at our disposal ordinarily carried appreciable numbers of clostridia in the substance of the liver. It must be noted that in experimental groups I to IV the specimens of liver taken for culture at the time of operation were small wedges from the margin of a lobe, whereas in Group V large masses (up to 50 gm.) were taken from the full thickness of the left lobe. Of the small wedges, only two were positive for the organisms. This serves to emphasize that the "normal" degree of contamination is not heavy. It seems justifiable to conclude that the immediate source of the blood and liver infection is the liver itself.

The groups of animals treated parenterally with penicillin and aureomycin served to demonstrate several further points. In the first place, to be effective, treatment had to be commenced at once on completion of the operation, or, still better, an hour before the operation took place. This was to be expected in view of the early onset and fulminating course of the infection. Secondly, the actual antibiotic used made little difference, provided the dosage was sufficient to produce a blood concentration to which the clostridia were sensitive.[6] Thirdly, the duration of treatment need not be prolonged beyond two days in order for the animal to survive. The penicillin preparation used was one known to provide adequate blood concentrations for approximately this interval.

The fact that a short period of protection is adequate suggests that some adaptive mechanisms exist. Apparently no severe or extensive pathological changes, such as infarction, are essential to the production of conditions for anaerobic growth, nor were we able to find definite evidence of infarction or thrombosis in any of the liver biopsy specimens taken during the postoperative period. Loeffler [7] has suggested that the role of the hepatic artery in the intrinsic blood supply

6. Samples of the clostridia obtained were found to be sensitive to penicillin in concentrations of 1 unit and to aureomycin in concentrations of 0.3 microgram, per cubic centimeter.

7. Loeffler, L.: Factors Determining Necrosis or Survival of Liver Tissue After Ligation of Hepatic Artery, Arch. Path. **21**:496 (April) 1936.

of the portal vein may be of such importance that necrosis and thrombosis of the portal veins will follow arterial ligation. Yet, if such drastic pathological changes are an essential part of the disease pattern, it is hard to visualize sufficient recovery being possible within 48 hr. to allow for survival without the further protection of antibiotics. It seems more likely that some adjustment in circulation must occur within that time to alter the balance toward better oxygenation. Time would also favor the numerous adaptive and protective mechanisms of the body as a whole.

A suggestive example of such adaptive mechanisms was noted in one animal which received one dose of penicillin (Dog 25). Blood and liver cultures became positive at four hours after operation. However, the animal did not die, as had all others with positive cultures. Cultures remained positive until the fourth day, although the animal appeared quite well. From the fifth to the fifteenth day, cultures were done and were all negative, and the animal was clinically recovered. The dog lived normally for two months and was then killed. Evidently the animal was tided over the first two days by the penicillin treatment and thereafter was able to suppress the infection by virtue of its intrinsic resistance.

In a group of further experiments, the results of which are too fragmentary to report in complete form, we obtained some evidence that the intrahepatic oxygen concentration is indeed lowered by interruption of the arterial supply. Our technique was to measure oxygen levels in the portal and hepatic veins before and after arterial interruption, while following the carotid arterial blood pressure. Results were so irregular as to suggest that some uncontrolled factor, perhaps autonomic nerve disturbance, was operating. Furthermore, abrupt changes in the clotting powers of the blood added to the technical difficulties. In general, however, reductions in the hepatic venous oxygen concentration of the order of 50% below control levels were obtained, without there being any simultaneous development of shock as judged by the peripheral blood pressure. It is felt that the rapid development of an overwhelming clostridial infection after arterial ligation is the result of a sudden change in the intrahepatic environment in the direction of less aerobic conditions.

SUMMARY

Complete interruption of the arterial supply to the liver of the dog led to early death of the animal. A bacteremia yielding a pure culture of an organism indistinguishable from Clostridium perfringens (Clostridium welchii) appeared two to three hours after the ligation and persisted until death. Specimens of liver obtained by the needle-biopsy method gave positive cultures of the same organism from three to four hours after operation until death. No evidence of infarction or thrombosis was observed in histological sections of such punch biopsies.

Autopsy showed severe, infective, gaseous necrosis of the liver, always severer in the left lobe. Large numbers of organisms were present.

Preoperative suppression of intestinal clostridia with succinylsulfathiazole (sulfasuxidine®) given by mouth failed to protect animals from death. The clinical and bacteriological course was identical with that of the controls. Penicillin administered by intramuscular injection protected the animals, provided that it was given at or just before the time of operation. Aureomycin given intravenously for 48 hr. resulted in absolute protection in two animals.

Cultures of large masses of the left lobe of the liver from healthy animals yielded Cl. perfringens in all cases.

CONCLUSIONS

It is concluded that the cause of death after complete interruption of the hepatic arterial supply in dogs is an overwhelming infection with an organism resembling Cl. perfringens. This infection is primary in the liver, which is lightly contaminated in the normal dog, but rapidly becomes systemic in character. A bacteremia appears well in advance of significant pathological changes in the liver. It is felt that the necrosis of the liver seen in untreated animals is the terminal consequence of sepsis. The fact that the liver is largely protected in the presence of an antibiotic indicates that widespread hepatic damage is not a necessary sequel of hepatic arterial ligation.

Advice and assistance in connection with the bacteriological studies was given by Dr. R. W. Reed, Department of Bacteriology, Dalhousie University, Halifax, N. S.

PARENTERAL AND INTESTINAL ABSORPTION OF ANTIBIOTICS IN TRAUMATIC SHOCK

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AND
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CINCINNATI

THE EFFECT of traumatic shock on the levels attained in the circulating blood and tissue fluids by various antibiotics after their oral, intramuscular, or intravenous administration is of obvious importance in the management of wounded persons. Antibiotic agents are generally of value in the localization, control, or attenuation of infections developing in contaminated wounds, but their effect necessarily depends upon adequate function of the organs involved in their absorption and excretion. The profound depression of all vital activities occurring during traumatic shock could conceivably have a marked effect on the absorption and maintenance of adequate blood levels of the antibiotics. Little information is available, however, regarding the influence of shock on the blood levels obtained.

A series of experiments has been conducted to measure the antibiotic blood levels obtained through gastrointestinal, intramuscular, and intravenous administration of antibiotics in anesthetized dogs kept in a state of shock produced by traumatizing a hind limb, and to compare these levels with results obtained in the same animals before shock was produced.

MATERIAL AND METHODS

A total of 46 healthy dogs, weighing 10 to 12 kg., were used as the experimental animals in this study. After anesthesia was produced by the injection of pentobarbital (nembutal®) sodium, the normal animals were given one of the antibiotics, and determinations of the blood levels were made from samples withdrawn from the external jugular vein one-half, one, two, three, four, and six hours later. Antibacterial assays were made by the serial dilution method, using suitable test bacteria. For penicillin, the test organism used was Bacillus subtilis, and for aureomycin, Bacillus cereus.

In the penicillin studies, observations were made both before and during shock in 16 dogs, 10 receiving the antibiotic orally and six intramuscularly. Similar observations were made in 23 other dogs receiving aureomycin, 10 receiving this agent orally, eight intramuscularly, and five intravenously. An additional seven dogs in shock who received penicillin were studied without earlier observations in the unshocked state.

Read at the Eighth Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

This paper is based on work done under a grant from the United States Army, Office of the Surgeon General.

From the Department of Surgery of the University of Cincinnati College of Medicine and Cincinnati General Hospital.

The animals were allowed to rest for two or more days between the first experiments conducted in the unshocked state and the second ones done during shock. In the latter, the animal was again anesthetized and a continuously recording mercury manometer was connected by a cannula to the right femoral artery (Fig. 1). The right hind limb was then struck 10 to 15 heavy blows with a lead hammer at intervals until the blood pressure fell to, and remained at or below, a level of 80 to 90 mm. of mercury. Thereafter, a quantity of penicillin or aureomycin identical to that formerly used for the dog was given in the same manner as previously. Blood samples were obtained at the same interval and from the same source. Throughout the

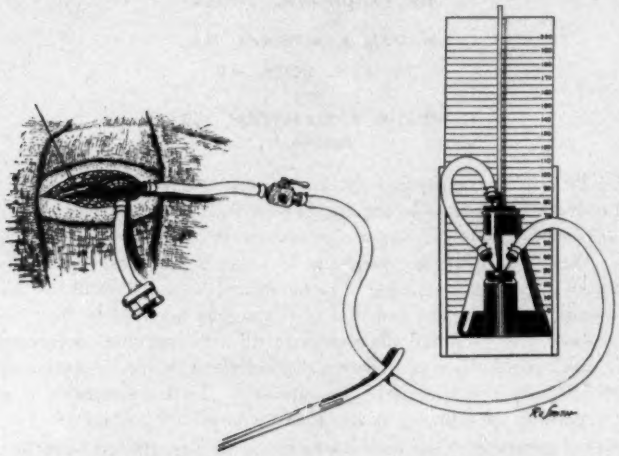

Fig. 1.—Drawing showing femoral vein of traumatized hind limb of anesthetized dog during shock with manometer attached.

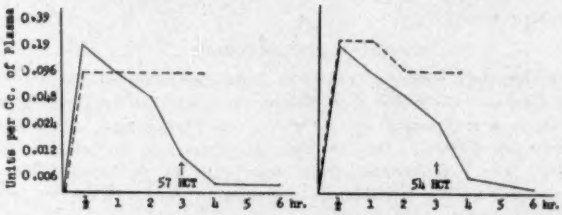

Fig. 2.—Comparison of penicillin levels developing in the blood of two dogs (No. 852, left, and No. 853, right) before and during traumatic shock. Solid lines indicate blood levels in normal dogs. Broken lines indicate blood levels in shocked dogs. *HCT* is hematocrit in volumes per cent. The dose of penicillin given was 40,000 units orally per kilogram of body weight.

experiment, the blood pressure of each animal was maintained at 80 to 90 mm. of mercury until shortly before death, when it fell rapidly. To maintain the state of shock, additional trauma was used if necessary.

In the penicillin experiments, a single dose of 40,000 units per kilogram of body weight was used for all the 16 dogs, the antibiotic being given orally in 10 and intramuscularly in six. A single dose of 40 mg. of aureomycin per kilogram of body weight was given orally or intramuscularly to 18 dogs. In five others a dose of 8 mg. of aureomycin per kilogram of body weight was injected intravenously. Large doses were used to produce consistently

measurable blood levels. Attempts were made to measure the urinary excretion of the two antibiotics, but they were unsuccessful because of the insufficient quantity of urine produced during the state of shock produced.

RESULTS

Both the oral and the intramuscular administration of penicillin in normal dogs produced peak blood levels in one-half hour. In the succeeding five and one-half hours, these levels fell continually and progressively to immeasurable levels (Figs. 2 and 3).

During shock, the oral administration of penicillin produced peak blood levels in one-half hour in 50% of the animals, while in the other 50% one hour was required

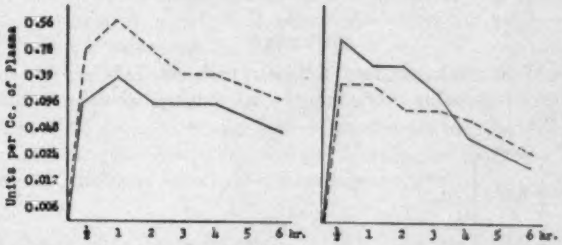

Fig. 3.—Comparison of rate of absorption, peak levels, and persisting concentrations of intramuscularly administered penicillin before and during shock in dogs No. 118 (left) and No. 119 (right). Solid lines indicate blood levels in normal dogs before shock, and broken lines, levels during shock. The dose of penicillin used was 40,000 units orally per kilogram of body weight.

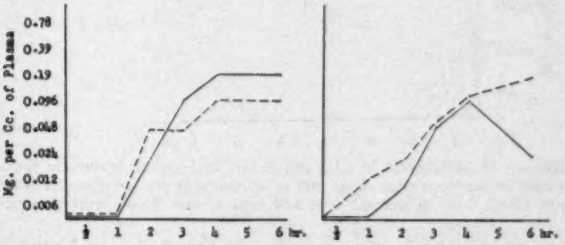

Fig. 4.—Comparison of blood levels occurring before and after shock in dogs No. 874 (left) and No. 869 (right), following a single oral dose of 40 mg. of aureomycin per kilogram of body weight. Solid lines indicate blood levels in normal dogs, and broken lines, blood levels after production of shock.

for maximum concentrations. However, in these dogs during shock, the blood levels fell more slowly and were actually higher in 70% of the instances during the following three to six hours.

The animals receiving the intramuscular injection of penicillin during shock required one to two hours for the development of peak levels, and again these levels fell more slowly, the final concentrations at the end of four to six hours being higher in every instance than normally.

The oral administration of aureomycin in normal dogs produced peak blood levels in two to three hours, and during shock the time required for this peak concentration was three to five hours (Fig. 4).

The intramuscular injection of aureomycin in normal dogs, as well as in the shocked animals, produced maximum concentrations in the blood within two to four hours. The blood levels during shock fell more slowly, and at the end of four to six hours the final levels of aureomycin were higher than normally.

The intravenous administration of aureomycin produced peak levels of aureomycin in the blood within one-half to one hour both before and during shock. Again the levels during shock fell more slowly, and the final concentrations were higher in every instance but one (Fig. 5).

Assays of the plasma-like fluid obtained from the traumatized limb showed penicillin and aureomycin to be present at the end of six hours in concentrations of approximately 0.24 to 0.48 unit, or microgram, per cubic centimeter.

COMMENT

An analysis of the results obtained in these experiments indicates that traumatic shock, even with its attending depression of vital activities, permits the absorption

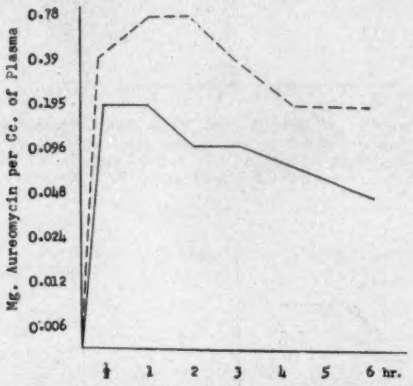

Fig. 5.—Comparison of aureomycin blood levels before and during traumatic shock in dog No. 930 after a single intravenous dose of 40 mg. of aureomycin per kilogram of body weight. Solid line indicates blood level in normal dog, and broken line, blood level in shocked dog.

of penicillin and aureomycin from the gastrointestinal tract after oral administration and from skeletal muscles after intramuscular injection. The evidence shows that the development of antibacterial levels may occur at the same rate in shock as in the normal state, but that in about one-half of the animals the development of maximum levels was retarded for one-half hour in the case of penicillin and one to two hours in the case of aureomycin. Of particular significance is the observation that the antibiotic levels fell more slowly and persisted at higher levels for longer periods of time during shock. Of more practical importance was the demonstration that the antibiotics were diffused into the traumatized tissue and tissue fluids in adequate concentration and with active antibacterial properties.

The knowledge that traumatic shock permits adequate absorption of the orally or parenterally administered antibiotics is of obvious importance at this time in planning for the care of great numbers of casualties which possibly might occur

during a short time. Under the conditions of a major catastrophe, such as an atomic attack, the oral administration of these or other antibiotics would be the most feasible, since sufficient medical personnel and supplies for parenteral injections would be generally unavailable. Oral administration by directed lay personnel or by many of the victims themselves could be done relatively easily. The intramuscular injection of aureomycin was very irritating locally and is not recommended for human patients.

SUMMARY

A group of experimental studies in 46 dogs indicated that traumatic shock did not prevent the absorption of penicillin or aureomycin after oral or parenteral administration, but the rate of absorption was retarded in 50% of the animals. The blood concentrations usually persisted at higher levels and for longer periods in the shocked state than during its absence.

Penicillin was absorbed more rapidly after oral or intramuscular injection than aureomycin both in the presence and in the absence of shock.

Penicillin and aureomycin were both diffused locally into the transudate accumulating at the site of injury in the shocked animals and were maintained there in sufficient concentrations for effective antibacterial activity.

LATE RESULTS OF SURGERY IN PERFORATED DUODENAL ULCER

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THE PERMANENCE of cure following the surgical treatment of perforated duodenal ulcers has long been the subject of much speculation. Throughout the literature there seems to be a note of extreme optimism, which suggests that the majority of persons who have had a perforation can look forward to a future free from ulcer distress. In one series published in 1936 the author states that 95% of the patients who underwent simple closure of a perforated ulcer remained well in the ensuing follow-up which extended over a 26 yr. period.

For many years now a group at the Toronto General Hospital have been especially interested in all aspects of the problem of perforated ulcers. In a former communication, published in 1944, we presented the details of the immediate management of 114 cases. In this paper I should like to describe what has happened to the patients in this series in a follow-up period which ranges from a maximum of 20 to a minimum of five years. There will also be given some concrete figures on the permanence of cure which has occurred in this series.

The group has always maintained, rightly or wrongly, that the surgeon's sole responsibility in the treatment of perforated duodenal ulcers is to save the patient's life and to do this with the simplest and quickest procedure at his disposal. Having accepted this premise, we have practised simple closure of the ulcer only and have seldom been faced with the necessity of performing any other type of operation, such as gastrectomy or gastroenterostomy. It is what I suppose may be called a conservative approach to the problem, for indeed excellent results have been obtained by some in the treatment of this lesion by immediate gastric resection.

For the sake of completeness in the ensuing discussion the salient points in our technique of closure are now presented. Once the perforation is visualized, three interrupted intestinal sutures are placed parallel to the long axis of the duodenum, one above, one below, and one across the center of the perforation. We then lay over the hole a piece of omentum either attached or detached, and tie the sutures just sufficiently tightly to hold the omental patch in position. No attempt is made to close the perforation with sutures first; they simply hold the omentum in place so that the patch, together with fibrin, can seal off the opening. If there is gross soiling of the peritoneal cavity, the exudate is sucked out and the abdomen closed without drainage. It is unnecessary to go into the postoperative routine, apart from stating that because this series extends only up to 1944 the results have not been influenced by the use of penicillin or streptomycin.

Read at the Eighth Annual Meeting of the Central Surgical Association, Chicago, Feb. 23, 1951.

After the above plan of treatment there were seven operative deaths in 111 cases. Three patients were not operated on; two refused operation, and the condition in one remained undiagnosed until a subsequent subphrenic abscess perforated into a bronchus.

The causes of death in the seven cases were briefly as follows: pulmonary embolus, occurring on the 15th day, one case; pneumonia, 3 cases; uremia, one case; unrecognized pelvic abscess which ruptured into the general peritoneal cavity, one case, and subphrenic abscess, which, as in the other case, perforated into a bronchus, one case. This gives an operative mortality of 6.3%.

What has happened in the ensuing years to the 104 patients who survived the operation? In view of certain findings in the follow-up study, it is interesting to note (1) that there were only six females in the group and (2) that 50% of all patients (male and female) were over 50 yr. of age at the time of perforation.

Eleven of the 104 patients have since died from causes unassociated with the gastrointestinal tract. As one might suspect, these fell into the older age group. The majority of deaths were due to cardiovascular accidents and the others to a variety of causes. Of the 11 patients, six had had typical or severe ulcer symptoms in the years prior to their death.

We have been unable to find any trace of another 15 patients, so that the total number of cases that we have been able to follow personally amounts to 78. An attempt has been made to classify these 78 cases according to groups, and the classification which seemed to be most valuable depended on the type of symptoms present at the time of follow-up study, as follows:

(1) Those who are asymptomatic—23%; (2) those with mild symptoms—8%; (3) those with typical symptoms—22%; (4) those with severe symptoms—12%; (5) those having undergone further operation—35%.

An easier classification is the following:

(1) Those with no symptoms or mild symptoms—⅓; (2) those with typical or severe symptoms—⅓; those having undergone further operation—⅓. One can see, therefore, that in our series, about one-third have little or no further trouble after perforation, another third have a moderate amount of trouble, and another third have bad trouble which has climaxed in further operative intervention.

The figures in this narrow classification were examined to see whether any outstanding conclusions could be reached. Numerous questions immediately arose which seemed to demand answers. In the first group, those with no symptoms or mild symptoms, we were interested in the following questions: 1. Did the age of the patient at the time of perforation have anything to do with the benign course in subsequent years? 2. Was the ulcer acute or chronic at the time of perforation? 3. Did this group have a low free acid postoperatively? 4. Did they follow a strict routine postoperatively, with diet, no smoking and no drinking?

In this first group the average age at the time of perforation was 49 yr. and at the time of follow-up, 57 yr. The average duration of ulcer symptoms prior to perforation was six and a half years. In the group, however, were five patients in whom symptoms were present for three months or less before operation. The average free acid in the test meal at the end of a two-week convalescent period was 50 units. Eighty-four of this group did not adhere to their diets; 77% of them smoked, and 65% of them drank alcoholic beverages.

To summarize, this group consisted mainly of men in the middle age group who had chronic duodenal ulcers of relatively long standing. In spite of an average free acid of moderate amount and in spite of the fact that the majority did not follow their diet and did smoke and drink, these men were well an average of eight years later.

Can any startling conclusions be reached? The figures show that a certain number of patients with duodenal ulcers which have perforated can get along perfectly well with no restrictions whatever. We cannot conclude much more than that, since one of the men whom we were going to include in this so-called well group was a man of 56 yr. who had gone 10 yr. after perforation with complete freedom from symptoms and no restrictions and in whom typical ulcer symptoms developed on the 11th anniversary of his perforation. Roentgenologic examination showed an active crater in the duodenum.

In the second group, those with typical or severe symptoms, the average age at the time of perforation was 42 yr. and at the time of follow-up 50 yr. The average duration of symptoms prior to perforation was five and a half years and the average free acid 48 units. Of this group, 72% did not follow their diets, 95% smoked and 60% drank.

When the two groups are brought together for comparison, the only feature of note is that those with severe symptoms are five years younger than the asymptomatic group and that 95% of the second group smoke, in contradistinction to 77% in the asymptomatic group. It may be well to note here that in this era of trial and trouble and unrest every patient who has suffered perforation of an ulcer since 1941 has had symptoms of ulcer on follow-up examination.

As far as the smoking and drinking are concerned, some may suggest that it is of no significance in any one group unless it is determined how much the patients indulge in this favorite pastime. We have gone into that question thoroughly and have found that those who had absolutely no symptoms at all drank and smoked more than those who had severe symptoms.

The first fact that stands out from examination of these two groups together is that while theoretically there is a medical type of postoperative management for perforated duodenal ulcers, the large majority of patients cannot or will not follow it. If this be true for an ulcer lesion which has demanded surgical operation, surely it is just as true for the so-called medical management of an uncomplicated ulcer which has never caused any serious trouble.

The second fact is that, from the age of the patient at the time of perforation, from the apparent acuteness or chronicity of the ulcer, from the amount of free acid postoperatively, or from the degree of adherence to dietary restrictions, one cannot predict with any degree of assuredness whether a patient will have trouble with his ulcer in the future.

Another one of the factors that we had hoped to determine with this follow-up was the possibility of discovering in the first year or two after operation those patients who would require another operation. For example, we wished to determine whether a patient who continued to have ulcer symptoms for six months or a year after closure of a perforation should be operated on. We have encountered a number of patients who had typical or severe symptoms in the first one to three years after perforation and who were advised to submit to gastrectomy but refused and were

perfectly well 10 yr. later. If the patients have symptoms of penetration, stenosis or bleeding, the decision is not hard to make. It seems, therefore, that, as in any other field of surgery, there is no hard and fast rule to be followed in the late treatment of a perforated ulcer. Each case must be treated on its merits.

The last group comprises those who have been operated on again subsequent to perforation. Of these, 22% underwent gastric resection, 6% gastroenterostomy, and 6% closure of another perforation. The reason for operation in the latter two groups is obvious. The gastroenterostomies were all performed for stenosis, which ensued in six months to two years after perforation.

A total of 18 patients were subjected to gastrectomy. In these, apart from two in whom pyloric obstruction was due to scar stenosis from an anterior wall ulcer, laparotomy revealed the site of the offending lesion to be on the posterior wall. Two possibilities should be considered here, (1) that an unrecognized posterior wall ulcer was present in conjunction with the anterior wall ulcer at the time of perforation and (2) that the same basic etiological factor which caused the original anterior ulcer had now caused a posterior one to form. Fifty per cent of the patients underwent their second operation in from two to six months after their perforation was closed and the remainder an average of two years later.

The reasons for performing the gastrectomy in these 18 cases are revealing. Eight had severe symptoms of a posterior wall ulcer penetrating into the pancreas, with persistent back pain. Four had marked pyloric obstruction. Three had one or more episodes of massive hematemesis. In two cases the ulcer had penetrated into the common bile duct and caused jaundice. In the final case, gastrectomy was performed because of the occurrence of a gastric ulcer. It can be seen, therefore, that the large majority of patients underwent resection not because of the original ulcer of the anterior wall but because of a coincident or subsequent posterior lesion. It will be noted that in 6% of the patients another perforation developed. These secondary perforations occurred from one to nine years after the original ones.

It is interesting to note what happened to a select group in the series, made up of the six female patients mentioned before. Three have undergone another operation (one gastrectomy, one gastroenterostomy and one closure of another perforation); two have typical ulcer symptoms, and one is dead from heart disease but had typical symptoms in the months prior to death.

Finally, in our examination at the time of follow-up we were most careful to examine the abdominal scars for the presence of incisional hernias and to try to correlate these hernias with the incidence of wound infections at the time of perforation. Twenty-seven per cent of the group followed who underwent simple closure of their ulcer without drainage of the abdomen or the wound later had a wound infection of mild to severe degree. Of those with wound infections, incisional hernias have developed in 25%, all in the group classified as "severe."

SUMMARY

We have attempted in the past two years to follow some 114 cases of perforated duodenal ulcers whose immediate management we had reported in 1944. The longest follow-up period was 20 yr. and the shortest five years. The operative mortality of the group was 6.3%. One-third of the 78 patients whom we have interviewed personally have little or no trouble with their digestive apparatus now. One-third

have typical or severe symptoms of ulcer characterized by pain, nausea and vomiting, or bleeding episodes. One-third have undergone further operative procedures, consisting of gastrectomy, gastroenterostomy or closure of another perforation.

Although theoretically there should be a medical plan for the postoperative management of these patients, in a large percentage of cases it is not carried through by the patient. It is evident that a certain number of patients can remain absolutely symptom-free after perforation and yet not follow any dietary rules or restrictions in smoking or drinking.

On the basis of this series the future of a female patient with a perforated ulcer is not too bright. The incidence of postoperative wound infection in the patients studied is high, but in spite of this the incidence of incisional hernia is not as great as might be expected.

Our group plans to teach and practice simple closure of perforated duodenal ulcers until we can be convinced that a better method of treatment is available.

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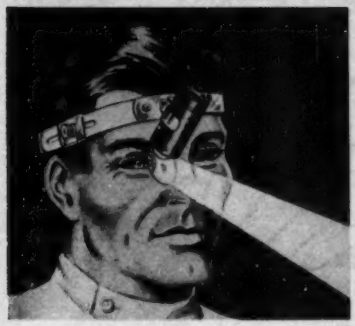

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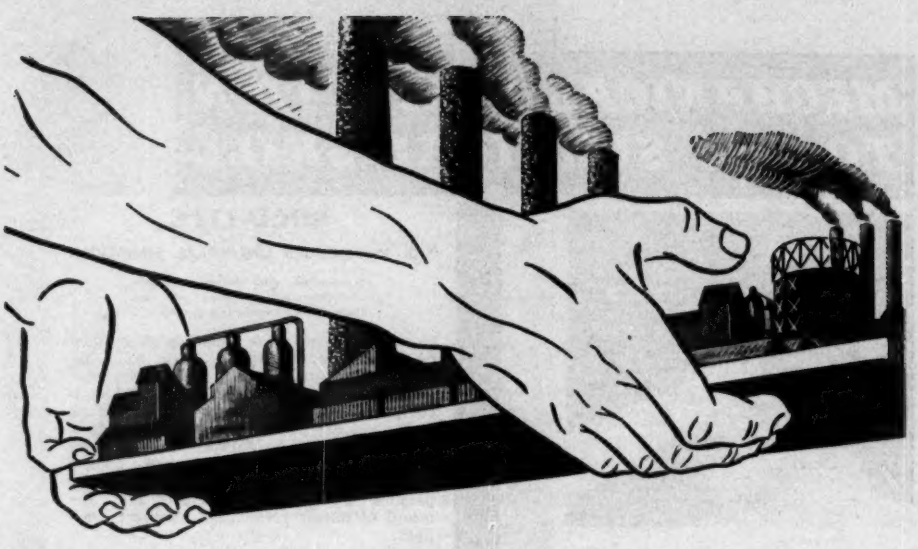

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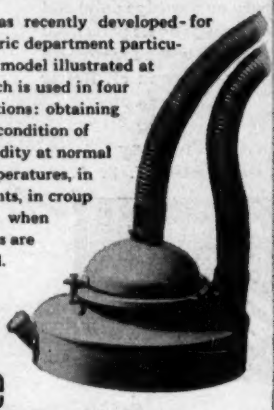

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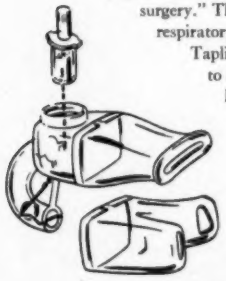

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1. Taplin, G., Cohen, S., and Mahoney, E. (1948), Prevention of Postoperative Pulmonary Infections, J. Amer. Med. Assn., 138:4, Sept. 4.

2. Krasno, L., and Rhoads, P. (1949), The Inhalation of Penicillin Dust; Its Proper Role in the Management of Respiratory Infections, Amer. Prac., 11:649, July.

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